UNIVERSIDADE DE LISBOA

FACULDADE DE MOTRICIDADE HUMANA

KNEE OSTEOARTHRITIS AND OBESITY : EFFECTIVENESS OF PICO AQUATIC EXERCISE PROGRAM ON SYMPTOMS, PHYSICAL FITNESS AND QUALITY OF LIFE

Dissertação elaborada com vista à obtenção do grau de Doutor em Motricidade Humana na especialidade de Atividade Física e Saúde

Orientador: Professora Doutora Maria Margarida Espanha

Coorientador: Professor Doutor Stephen Messier

Júri:

Presidente:

Reitor da Universidade de Lisboa

Vogais:

Doutor Jaime da Cunha Branco

Professor Catedrático da Faculdade de Ciências Médicas da Universidade Nova de Lisboa

Doutor José Henrique Fuentes Gomes Pereira

Professor Catedrático da Faculdade de Motricidade Humana da Universidade de Lisboa

Doutora Maria Joana Mesquita Cruz Barbosa de Carvalho

Professora Associada com Agregação Faculdade de Desporto da Universidade do Porto

Doutora Maria Margarida Marques Rebelo Espanha

Professora Associada da Faculdade de Motricidade Humana da Universidade de Lisboa

Doutora Maria Helena Santa Clara Pombo Rodrigues

Professora Auxiliar da Faculdade de Motricidade Humana da Universidade de Lisboa

FLÁVIA GIOVANETTI YÁZIGI

Julho de 2014

The work presented in this dissertation was supported by the Portuguese Foundation for Science and Technology (scholarship: SFRH/BD/46425/2008).

FCT Fundação para a Ciência e a Tecnologia

MINISTÉRIO DA EDUCAÇÃO E CIÊNCIA

Declaração de Reprodução da Tese

Nome: Flávia Giovanetti Yázigi

Endereço eletrónico. fyazigi@fmh.ulisboa.pt Telefone: 214149159

Número do Cartão de Cidadão: 15918029

Título: Obesity and knee osteoarthritis : Effectiveness of PICO aquatic exercise program on symptoms, physical fitness and quality of life.

Orientador: Maria Margarida Espanha

Coorientador: Stephen Messier

Ano de conclusão: 2014

Doutoramento: Motricidade Humana na especialidade de Atividade Física e Saúde

Faculdade de Motricidade Humana – Universidade de Lisboa

Cruz Quebrada, 11/ 06 / 2014

Assinatura ______________________

Para as estrelas que me guiam,
Roberto Yázigi e Sabina Gozzi Giovanetti

Para a minha mãe, Amalia Yázigi
Mesmo distante, sempre presente
Ensinaste-me a acreditar
És o meu eterno pilar

A ti, minha filha Debora, que esta tese lhe sirva de exemplo.
Tudo tem seu tempo, nada é em vão
Com trabalho, dedicação e resiliência
conseguiras tudo aquilo a que te propuseres,
da melhor forma que puderes

Um brinde à vida!

Acknowledgements

When a person read this present document maybe everything will look very simple, clear and easy. Even for me, when I look backward the past became simple now. Only a person who lived similar process can understand the unimaginable conflict of feelings in which we are constantly confronted. The really true is that this thesis involved a very complex process which was not possible without the interaction of different labs and with and enormous human friendship.

In this way I would like to express my sincere acknowledge to the many person who had contributed in different ways to makes this thesis possible.

I cannot find words to express my gratitude to Professor Margarida Espanha. I would recognize her guidance, an everlasting encouragement and friendship, which supported me across this discovery and learning phase.

My special words to Prof Stephen Messier and all staff from Wake Forest University for having received me. Thank you for relevant insights provided to this investigation and also, for welcomed and supported my pregnancy stage.

I would also like to thank to Dr. Filomena Carnide for supervising my first study, the KOPS validation, to Dr Filomena Vieira, Dr Cristina Bento and Dr Antonio Veloso for their participation in this work supplying scientific knowledge.

I am very grateful to Dr Pedro Teixeira for giving me the opportunity to work with PESO Comunitario.

To PICO staff (André, Carlota, Joana e Ines), to aquatic exercise instructors from our faculty (Francisco, Susana, Joana e Iola) and to all volunteers, thank you, none of this would be possible without your commitment.

Thanks to my colleagues for any kind of motivation or support during this phase of my life. Espadinha, Adilson, Filomena, your availability to help is indescribable.

An special word to all my friends, you know how I respect and valorize your friendship, thank you to be in my way.

Finally, I would like to recognize the effort of my family to accompany me, giving me an enormous understanding and love in challenging times.

Institutional acknowledgements

Without institutional support, the PICO project would not be possible. In this way, I would like to thank to the Portuguese Institute of Rheumatology for the clinical diagnosis, to the Instituto Português do Desporto e Juventude, which provided the swimming pool, for the classes realization and also, to the laboratories of Faculdade de Motricidade Humana (Biomechanics and Functional Morphology lab, Health and Exercise lab and Biochemistry and Exercise Physiology lab), which supported the tests realization. Additionally, my thanks for Fundação da Ciência e Tecnologia, for my scholarship (SFRH/BD/46425/2008).

Abstract

Background: Aquatic exercise is a nonpharmacologic intervention recommended for knee osteoarthritis (KOA) management. This study aimed to determine the effectiveness of 3-months of aquatic exercise program on KOA symptoms, physical fitness, and quality of life in overweight/obese adults with KOA. **Methods:** Eligibility criteria were 40 ≤ age ≤ 65 years; BMI ≥ 28 kg/m^2; clinical and radiographic KOA. Participants were randomized in aquatic exercise group (AEG) and control group (CG). Physical Fitness was assessed by Six Minutes Walking Test (6MWT), Chair Sit and Reach Test (CSR), Five-Repetition Sit-To-Stand Test (FRSTST), Handgrip Strength Test (HST) and isokinetic and isometric knee strength tests. KOA symptoms and quality of life were assessed by self-reported questionnaires (Knee Injury and Osteoarthritis Outcome (KOOS), Brief Pain Inventory (BPI), Beck Depression Inventory (BDI), International Physical Activity Questionnaire (IPAQ), Weight and Lifestyle Inventory (WALLI). Body composition and morphology was measured by DXA scanner and waist, hip and thigh circumferences. Descriptive statistics and Pearson Correlation Coefficient were used for baseline analyses; Univariate Analyses of Covariance (ANCOVA) was used as primary analyses. **Results:** Final sample included 48 adults (BMI: 35.0±4.9 kg/m^2; age: 55±7 years.), 23 in the CG and 25 in AEG. Regarding physical function, significant group effect was found for 6MWT, FRSTST (p<.001) and Isokinetic flexion peak torque, in both knees (p<.05). Regarding KOOS; BPI and BDI, significant group effect was found in all dimensions. **Conclusion:** PICO aquatic program was effective in improving KOA symptoms, physical fitness and health-related quality of life of its practitioners. **Trial Registration:** NCT01832545

KEY WORDS: Aquatic Exercise; Knee Osteoarthritis; Pain; Obesity; Physical Fitness

Resumo

Introdução: O exercício aquático é considerado uma opção não farmacológica no tratamento e controlo dos sintomas da osteoartrose do joelho (OAJ). O principal objetivo deste estudo foi determinar a eficácia de um programa de 3 meses de exercício aquático nos sintomas, aptidão física e qualidade de vida de adultos com sobrepeso ou obesos com OAJ. **Métodos**: Os critérios de elegibilidade foram 40 ≤ idade ≤ 65 anos; IMC ≤ 28 Kg/m^2 e diagnóstico clínico e radiológico de OAJ. Os participantes foram randomizados em grupo de exercício aquático (GEA) e grupo controlo (GC). Aptidão física foi avaliada pelos testes de Seis Minutos Marcha (6MM), Sentar e levantar da Cadeira 5X (SLC), Sentar e alcançar, Alcançar atras das costas, força de preensão manual e avaliação isométrica e isocinética da força dos músculos do joelho. Os sintomas e qualidade de vida foram avaliados por questionários de autorrelato: Questionário KOOS sobre o Joelho, Inventário Breve da Dor (IBD), Inventario de Depressão de Beck (IDB), Questionário Internacional de Atividade Física (IPAQ), Inventário do Peso e estilo de vida (IPEV). A composição corporal e morfologia foram avaliados por DEXA *scanner* e medidas de circunferência. Estatística descritiva, coeficiente de correlação de Pearson, análise Univariada de covariância (ANCOVA) e regressão linear múltipla foram os métodos estatísticos utilizados. **Resultados**: 48 adultos (IMC: 35.0±4.9 Kg/m^2, idade: 55±7 anos) completaram o estudo, 23 no GC e 25 no EAG. Quanto à função física, foi encontrado efeito de grupo significativo no 6MM, SLC (p<.001), no pico de torque da força de joelho na flexão, em ambos os joelhos (p<.05). Efeito de grupo significativo foi encontrado nas dimensões do KOOS; IBD e IDB. **Conclusão:** O programa aquático PICO foi eficaz para promover a melhoria dos sintomas da OAJ, da aptidão física, estado psicológico e qualidade de vida relacionada com a saúde de seus praticantes. **Registro de *Clinical Trial***: NCT01832545

PALAVRAS-CHAVE: Exercícios aquáticos; Osteoartrose do joelho; Dor; Obesidade; Aptidão Física

Table of Contents

Tables

Figures

Abbreviations

ADL	Activities of Daily Living
AE	Aquatic Exercise
AEG	Aquatic Exercise Group
BDI	Beck Depression Inventory
BM	Body Mass
BMI	Body Mass Index
BPI	Brief Pain Inventory
CG	Control Group
CSRT	Chair Sit and Reach
DXA	Dual Energy X-ray Absorptiometry
EXT	Extension
FLEX	Flexion
FM	Fat Mass
FRSTST	Five Repetitions Sit to Stand Test
HR	Heart Rate
IPAQ	International Physical Activity Questionnaire
ISOM	Isometric
KOA	Knee Osteoarthritis
KOOS	Knee injury and Osteoarthritis Outcome Score
LPK	Least Painful Knee
MET	Metabolic Equivalent of Task
MOM 1	Baseline
MOM 2	After 12 weeks of intervention
MPK	Most Painful Knee
NRS	Numerical Rating Scale
OA	Osteoarthritis
PAL	Physical Activity Level
PGIC	Patient Global Impression of Change Scale
PkTQ	Peak Torque
6MWD	Six Minutes Walking Distance
6MWT	Six Minutes Walking Test
VO_{2max}	Maximal Oxygen Consumption
WALLY	Weight and Lifestyle Inventory

Chapter 1: Introduction

This chapters presents the dissertation structure and the list of abstracts and works related to the PICO project (Intervention Program Against Osteoarthritis).

2

1.1 Overview

Rheumatic diseases (RD) include over 150 disorders, and although death rates are low, they are one of the primary causes of compromised quality of life and absenteeism from work, with significant economic and social consequences[1].

In Portugal, RDs are responsible for 40 to 60% of cases of prolonged physical incapacity in daily activities, 43% of absenteeism from work, and 35 to 41% of early retirement due to illness[2]. The prevalence of rheumatic diseases, both in Portugal and worldwide, is increasing, with significant repercussions for public health.

Following the establishment of the “Bone and Joint Decade” by the World Health Organization (WHO)[3], the Portuguese government established the National Program Against Rheumatic Diseases (2004 – 2010), which aimed to improve the quality of life of patients with arthritis[2]. This was followed by the creation of the ONDOR (*Observatório Nacional contra as Doenças Reumáticas* or National Observatory Against Rheumatic Diseases)[4] in 2003 by the Portuguese Society of Rheumatology and the Faculty of Medicine of Porto. Since that time, the ONDOR has published two books with reports of their work, “O estado da reumatologia em Portugal”[5] and “Doenças remáticas em Portugal: da investigação às políticas de saúde” [6]. The Portuguese Epidemiologic Study of Rheumatic Diseases (EpiReumaPt), started in 2014, is an ongoing, national, population-based, cross-sectional, epidemiologic study to estimate the prevalence of rheumatic diseases and health-related quality of life in Portugal.

According to the WHO[1], rheumatoid arthritis, osteoarthritis, osteoporosis, spinal disorders and severe limb trauma are the osteoarthritis (OA) conditions with the greatest impact on society and risk to an individuals’ quality of life, leading to loss of autonomy and incapacity, and are becoming a serious international public health problem. Because the knee is the most affected weight bearing joint[7], there is a high prevalence (11.1%) of knee osteoarthritis (KOA) in the Portuguese population[8].

Obesity, prior knee injury, physical activity levels, lower limb strength and the extent of alignment/misalignment of body segments are the most often cited potential risk factors for KOA. In Portugal, more than 50% of the population is overweight or obese[9], and this value is expected to increase as the rate of obesity[10] increases and the population ages[11].

The guidelines for KOA management include recommendations for a combination of pharmacological and non-pharmacological approaches. Exercise is considered an effective non-pharmacological treatment and is recommended by the Osteoarthritis Research Society International (OARSI)[12-14], the American College of Rheumatology (ACR)[15] and the European League Against Rheumatism (EULAR)[16]. Among exercise modalities, aquatic exercise can play an important role in reversing the framework of loss of functionality and in controlling OA symptoms [12-14]. However, there are few published articles with detailed aquatic exercise protocols, and these studies have not been consistent with respect to the methodologies used and populations studied.

The present dissertation, entitled "Obesity and Knee Osteoarthritis: Effectiveness of PICO aquatic exercise program on symptoms, physical fitness and quality of life" is a result of the PICO project (Intervention Program Against Osteoarthritis / Programa de Exercício Contra a Osteoartrose) that aimed to develop an adequate aquatic exercise program for obese individuals with KOA.

1.2 Dissertation structure

The organization of this dissertation is intended to provide a fluid and continuous overview of the effects of an aquatic exercise program on pain and functional capacity of overweigh/obese individuals with KOA. Articles or abstracts related to this work that have been previously submitted or published can be found in the appendices. This dissertation is organized as follows:

- **Chapter 2** includes a literature review of the topic, highlighting general characteristics of KOA, its constraints and how exercise is related to KOA management. In addition, there is a review of the current literature regarding aquatic exercise programs, along with the main gaps that currently exist regarding the study of aquatic exercise effects on KOA.
- **Chapter 3** presents the aims of the study that supported this project.
- A detailed review of the methodology used in the study is described in **Chapter**

4. Two articles included in the appendices describe specific methodologies.

- In **Chapter 5,** the results of the study are organized into three parts. The first part presents sample characterization and data analyses for baseline outcomes. The second part has the analysis of the effectiveness of aquatic exercise and the third part includes all complementary analyses.

- **Chapter 6** contains a general discussion that provides a summary and integrated discussion of the main findings obtained in this study. This chapter is organized into three parts as described in Chapter 5 (results).

- **Chapter 7** contains the conclusion, research findings, practical implications and suggestions for future studies

- The **Bibliographic references** are presented after chapter 7, at the end of document, in a numbered format.

- **Appendices** are after the References section and include all material that is cited throughout the dissertation and that is essential to the integrity of the work presented. All submitted or published articles related to this project are also included.

1.3 Publications that are related to the dissertation

1. Yázigi F, F. C, Espanha M: **Development of the Knee OA Pre-Screening Questionnaire (KOPS) (under review).** *Int J Rheum Dis* 2014.
2. Yazigi F, Espanha M, Vieira F, Messier SP, Monteiro C, Veloso AP: **The PICO project: aquatic exercise for knee osteoarthritis in overweight and obese individuals.** *BMC Musculoskelet Disord* 2013, **14:**320.1.
3. Yázig F, M. E, Marques A, Vitorino J, Silva I, Sousa M, Cunha C: **Predictive Factors of 6MW Test in Obese Individuals with Knee OA.** *Acta Reumatol Port* 2012, **37:**66-67.Suppl.
4. Cunha C, Vieira F, Yázigi F, Espanha M, Carnide F: **Influence of physical activity and pain levels on lower limb morphology in obese adults with Knee OA .** In *International Convention on Science, Education and Medicine in Sport Glasgow, UK*. 2012.

Chapter 2: Literature Review

Topics in the literature review are presented from a general overview about KOA, highlighting general characteristics of KOA, its relation with obesity and quality of life. Thereafter, literature support about exercise in the KOA management and specificities about aquatic exercise are presented.

8

2.1 Knee Osteoarthritis

Although rheumatic diseases (RD) have low death rates, they are one of the primary causes of compromised quality of life and absenteeism from work, with attendant economic and social consequences[5, 17]. In Portugal, RD are responsible for 40 to 60% of cases of prolonged physical incapacity in daily activities, 43% of cases of absenteeism from work, and 35 to 41% of early retirements due to illness[2].

Osteoarthritis (OA) is the most prevalent rheumatic disease and represents a great risk to the quality of life of the individual due to its effect on lower extremity based activities (such as walking up and down stairs, climbing and squatting)[17-19] and the consequent loss of autonomy. OA is considered a disease of the whole joint that may result from multiple pathophysiological mechanisms[20] and involves joint degeneration, including degradation of articular cartilage and subchondral bone[5, 21, 22], which can lead to bone sclerosis and formation of bone cysts and marginal osteophytes (Fig. 1).

The causes of OA are not completely understood but it is thought to be a complex, adaptive response of the joints to biomechanical, genetic and environmental events [23]. In OA, imbalances in subchondral bone turnover can lead to thickened, low-quality bone, which contributes to cartilage loss, joint space narrowing and thinning of the trabecular bone[24].

OA signs include molecular, morphological, biochemical and biomechanical changes in both cells and the extracellular matrix, which lead to tissue softening, fibrillation, ulceration, loss of articular cartilage, sclerosis, and eburnation of subchondral bone, osteophytes and subchondral cysts. Recent studies have demonstrated that low-grade inflammation plays a pathophysiological role in OA. The severity and symptoms of OA, as well as its progression and the consequent impairment in physical fitness, may be mediated, in part, by the extent of chronic inflammation[25, 26]

In general OA affects knees, hips, hands and spine joints; however, the knees are the most commonly affected weight bearing joint[7]. Knee osteoarthritis (KOA) can compromise an individual's quality of life and exhaust considerable healthcare resources, making this rheumatic disease a stand out among the public health problems in many countries[27-29]. In Portugal, the National Observatory for the

Rheumatic Disease (ONDOR) reported a prevalence of KOA in the Portuguese population of 11.1% (IC95%: 9.4-13.1)[8], and this value is expected to increase due to increases in obesity [10] and an aging population[11].

KOA can occur in both joints of the knee, patellofemoral and tibiofemoral joints, but it is more common in the medial tibiofemoral compartment, most likely because the medial compartment bears 60–80% of the compressive loads in the neutrally aligned knee during normal walking[30] and because of the higher frequency of varus malalignment[31].

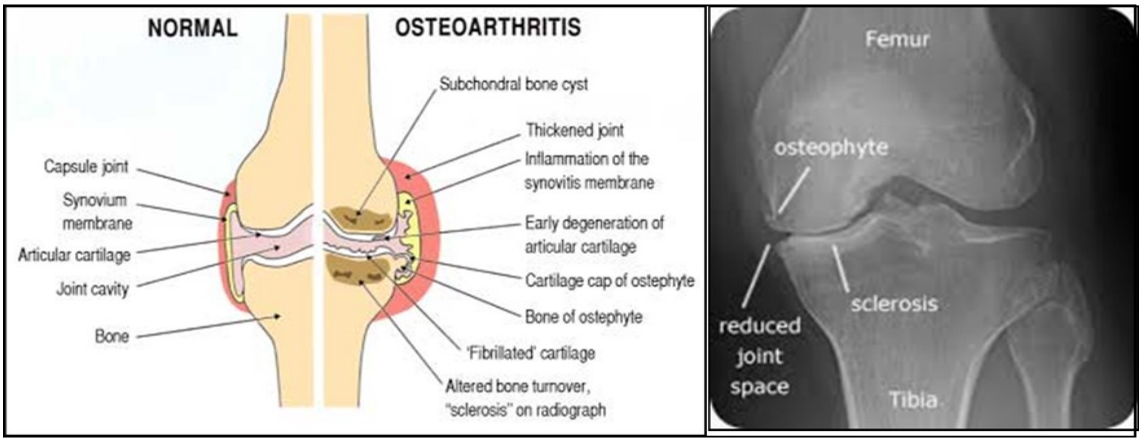


Fig. 1. Knee (http://en.wikipedia.org/wiki/Knee) and RX of a primary osteoarthritis of the left knee. Note the osteophytes, narrowing of the joint space (arrow), and increased subchondral bone density (arrow).

Age, obesity, occupation, lower limb muscle weakness, previous knee injury and misalignment are the main KOA risk factors reported in the literature, however, only obesity, occupation and strength are considered modifiable factors[32-35]. In the predictive model presented by Zhang and coworkers (2011)[36], six risk factors were related to KOA incidence (age, sex, BMI, occupation, family history and knee injury) and four risk factors were related to KOA progression (age, sex, knee injury and sports). Inflammation and biomechanical factors, such as joint loading, are also recognized risk factors that can exacerbate the progression of KOA [37-39].

2.1.1. Symptoms and quality of life

When clinically evident, KOA causes joint pain, tenderness, functional impairment, morning joint stiffness, joint position stiffness, crepitus, occasional effusion and variable degrees of inflammation without systemic effects[40]. In general, these symptoms compromise both joint stability and the capacity to perform movements during daily activities.

Pain is the main symptom of KOA and can result from the wear of the subchondral bone, which is widely innervated[41], or from local factors, such as synovial inflammation caused by by-products of cartilage degradation. The manifestation of this pain can have a mechanical or an inflammatory pattern[42]. Mechanical pain is related to knee joint movements and weight-bearing activities, intensifying with increased knee joint strain and disappearing after short rest. Additionally, it can increase with prolonged periods of inactivity, and can disappear after some gentle movement of the joint.

The occurrence of inflammatory pain is less predictable, is often described as burning, may be accompanied by swelling and a sensation of warmth, and can be increased by different factors[42]. Synovitis may activate sensory nerves, leading to pain symptoms and neurogenic inflammation[20]. Pain can inhibit muscle activity and, therefore, contribute to the loss of strength, alterations in loading, and changes in gait velocity [43, 44]. Although arthrogenic muscle inhibition (AMI) has been well documented after knee joint injury, pain and excessive intra-articular fluid, which is associated with the inhibition of alpha motor neurons due to abnormal afferent information from sensitized articular receptors, also compromise the ability to fully activate the quadriceps and hamstring muscles in KOA[45, 46].

The World Health Organization's definition of Quality of Life (QOL) is a broad ranging concept that is affected in a complex way by the person's physical health, psychological state, level of independence, social relationships, personal beliefs and their relationship to salient features of their environment[47].

The symptoms of KOA can deeply affect a patient's QOL; therefore, the implementation of interventions to control these symptoms and improve overall quality of life should be considered. In this dissertation, the dimensions of the patient's life that were considered with respect to their level of health and QOL included physical well-being, functional ability, emotional well-being, and social well-being[48].

2.1.2. Screening/Diagnosis

The resources available for KOA diagnosis include clinical evaluations (specialist examination and questionnaires) and biochemical or imaging methods[49-51]. The American College of Rheumatology (ACR) established three levels of diagnostic criteria for KOA: clinical only (92% sensitivity; 75% specificity), clinical and radiological (95% sensitivity; 69% specificity) or clinical and laboratorial (91% sensitivity; 86% specificity)[49].

Considering financial constraints, the clinical diagnostic criteria are the most viable option for primary care. According to the clinical criteria, KOA diagnosis should be based on the presence of knee pain in combination with at least three of the following variables: age>50, short-lived morning stiffness (<30 min), crepitus, tenderness, bony enlargement and no palpable warmth[49]. More recent recommendations from the European League Against Rheumatism (EULAR) for clinical KOA diagnosis are based on three symptoms (persistent knee pain, morning stiffness and functional impairment) and three clinical signs (crepitus, restricted movement and bony enlargement)[52]. A recent study concluded that crepitus could be an important symptom for detection of KOA progression in the patellofemoral joint[53].

Laboratory and imaging methods are costly and the connection between the results and KOA symptoms are not clear, particularly in the initial stages (pre-radiographic KOA, Kellgren-Lawrence radiographic grade 1)[54]. Although x-rays alone can provide a bone overview, the Kellgren-Lawrence (K-L) severity index is considered a useful method for KOA detection in epidemiological studies [55]. Magnetic resonance imaging (MRI), despite being a very expensive technique, is a sensitive tool that can identify joint components and some cartilage degeneration in the early stages[51, 56, 57]. According to Schipohof and coworkers[58], the MRI definition for tibiofemoral osteoarthritis (definite osteophyte and full-thickness cartilage loss or a combination of these factors with other MRI OA features) is a more sensitive method for detecting structural KOA than the Kellgren-Lawrence method[58]. However, more studies are necessary to verify which MRI findings in early OA are clinically important[53, 59].

For public health purposes, self-report questionnaires are still considered a valid and accessible method for KOA screening, but it is necessary to improve diagnostic instruments to ensure that interventions occur in the early stages.

The available KOA-related questionnaires can be organized into two groups: patient outcomes and screening instruments. The first group includes questionnaires related to patient outcomes (functionality, signs, symptoms and quality of life)[60-65], while the Western Ontario and McMaster Universities Arthritis Index (WOMAC)[60] and the Knee Injury and Osteoarthritis Outcome Score (KOOS)[62, 66] are widely used screening instruments.

The WOMAC has been validated with three types of scales: visual analog[60], Likert[60] and a numerical rating scale (NRS)[67]. The NRS allows an immediate evaluation and can be used on the phone or with a computerized touch screen (pain: Intraclass Correlation Coefficient (ICC)=0.915, rho=0.88; stiffness: ICC=0.745, rho=0.77, function: ICC=0.940, rho= 0.87).

The KOOS is considered an extension of the WOMAC and is a specific instrument developed to assess patients' perceptions about their knees, functional status and knee-related quality of life. The KOOS was validated with a sample of 21 participants with Anterior Cruciate Ligament (ACL) injuries. Its test-retest reliability after a 9-day interval showed an ICC of 0.75 for the Daily Living subscale (ADL), 0.81 for the Sport and Recreation subscale (Sport/Rec), 0.86 for the knee-related Quality of Life subscale (QOL), 0.85 for the Pain subscale and 0.93 for the Other Symptoms subscale[62] (O.Symptoms). The KOOS's responsiveness over 6 months was verified by assessing the effect size (QOL=1.65; Pain=0.84; ADL=0.94; O.Symptoms=0.87 and Sport/Rec=1.16)[62]. The construct validity of the KOOS was assessed in comparison to the SF-36 questionnaire[66].

2.2 Obesity and Knee Osteoarthritis

Knee Osteoarthritis (KOA) is highly prevalent in obese individuals[32]. The analyses published in 2010 by International Obesity Task Force (IOTF)[68], a part of the International Association for the Study of Obesity (IASO), estimated that, worldwide, approximately 1.0 billion adults are currently overweight and a further 475 million are obese.

In Portugal, more than 50% of population are overweight ($25<BMI\leq29.5$ kg/m^2) or obese ($BMI\geq30$ kg/m^2), with a prevalence in adults (18-64yrs) of 66.6% (males) and 57.9% (females) and a prevalence in older adults (≥65yrs) of 70.4%

(males) and 74.7% (females)[9]. With increasing rates of obesity[10] and the aging of the Portuguese population[11], the expectations are that the prevalence of KOA will increase.

There is a bidirectional interaction between KOA and obesity (Fig. 2) where weight load exacerbates mechanical pain, a symptom that markedly affects the individual's quality of life. Mechanical pain can cause irritability, sleeplessness, depression[69], and physical and psychological changes that may aggravate the disease, providing a general loss of functionality and, thereafter, inactivity. The majority of patients with KOA do not achieve the recommended levels of physical activity[14, 70], which can lead to weight gain and obesity[71]. The combination of obesity and KOA creates a vicious cycle of pain, physical activity reduction, loss of functionality, and disease progression leading to more physical activity avoidance[72], weight gain and increased pain. These cycles can be worsened with depressive symptoms, which are associated with obesity and KOA symptoms[69, 73, 74], where each can trigger and influence the other, further compromising the quality of life.

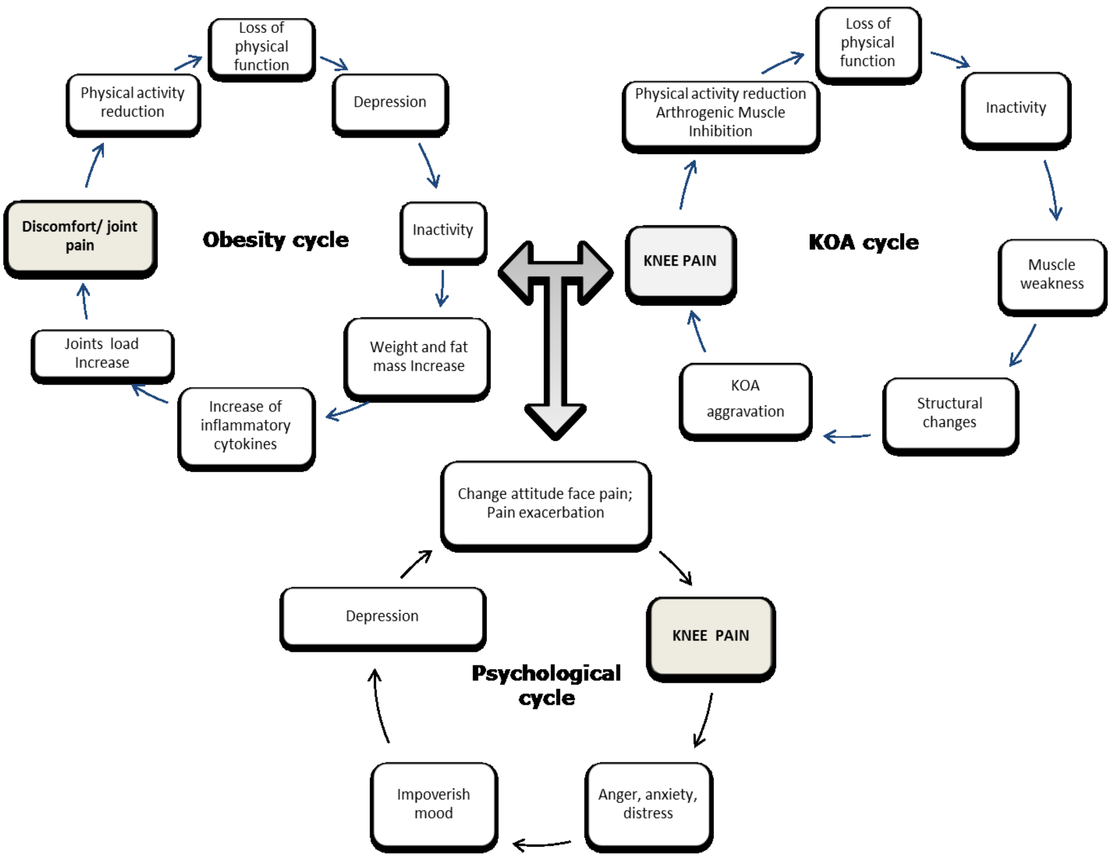


Fig 2. Bidirectional relationship between obesity and KOA cycle

In addition to local effects due to increased joint loading, obesity has systemic metabolic effects in KOA[75] caused by the higher concentrations of inflammatory markers (such as TNF-α and leptin) that are predominantly secreted by adipose tissue in obese individuals. These, in turn, can induce the production of IL-6 and C-reactive protein (CRP)[76]. The pathogenesis of obesity is characterized by hypothalamic inflammation and a subsequent, central resistance to leptin, which compromises the normal role of high leptin concentration to reduce food intake and increase energy expenditure. In addition, leptin increases the synthesis of TNF-β, a stimulator of osteophyte formation[77]. The resulting low-grade inflammation plays a pathophysiological role in OA because it can affect muscle function, lower the individual's pain threshold, and affect chondrocyte homeostasis, leading to degenerative changes in cartilage[25, 38, 78].

Weight loss in the prevention[34] and treatment of KOA is gaining increasing importance[12] because it provides a reduction in the load exerted on the knee during daily activities and can decrease the pro-inflammatory action of cytokines and adipokines, which are strongly activated by obesity[79-82]. Furthermore, in addition to reductions in pain manifestation, obesity is a controllable risk factor and decreasing its occurrence should contribute to a reduction in KOA progression.

Walking is one of the most important functionalities of the human being and is essential for autonomy and an independent life[83]. The aerobic capacity and walking ability in different populations have been evaluated by the Six Minutes Walking Test (6MWT), and reference values related to obesity and KOA have been published[36, 84-88].

Walking, as well other weight bearing movements, is the most common exercise pattern recommended for obese individuals when initiating their weight loss exercise program, however, the existence of knee pain and other KOA symptoms could be a constraint for exercise motivation and adherence, especially if symptoms of depression are also present[69, 89].

2.3 Exercise on Knee Osteoarthritis

The recommendations for KOA management include pharmacologic and non-pharmacologic approaches[12-15]. In general, and according to ACR[15], pharmacologic modalities can include acetaminophen, oral and topical NSAIDs, tramadol, and intra-articular corticosteroid injections.

Exercise is an effective non-pharmacological treatment for the management of KOA and is recommended by the Osteoarthritis Research Society International (OARSI)[12-14], by the American College of Rheumatology (ACR)[15] and by the European League Against Rheumatism (EULAR)[16]. Other non-pharmacologic modalities include weight loss in overweight patients, medial wedge insoles for valgus KOA, subtalar strapped lateral insoles for varus KOA, medially directed patellar taping, manual therapy, walking aids, thermal agents, tai chi, self-management programs, and psychosocial interventions [12-15].

Aerobic, aquatic and resistance exercise have been shown to help interrupt the cycle of pain-physical activity reduction, control KOA symptoms, improve posture and physical fitness[15], and act to modify risk factors such as body mass index (BMI) and muscle weakness[71]. However, the benefits of an exercise program depends on participant adherence, which, according Bennel (2011)[90], is very difficult to achieve in individuals with KOA symptoms.

Several reports indicate that an exercise program for KOA should be a broad intervention that includes cardiorespiratory training[15, 91, 92], lower limb strengthening[93-97], flexibility[83, 90], gait training[83, 98], and balance and posture training[99]. In addition, weight reduction (in cases of obesity)[12, 35], patient education[13, 15] and a psychological approach should be considered [73, 92]:

- Cardiorespiratory training: Aerobic exercise is one of the main physical fitness components and is correlated with an improvement in cardiovascular and respiratory function, a reduction in cardio-metabolic disease risk factors and a reduction in morbidity and mortality[100]. In addition to providing individuals with KOA the ability to perform daily living activities that require sustained aerobic metabolism[101], cardiorespiratory training has been shown to effect pain control[15] and reduce disability[91]. The Six Minutes Walking test has been widely used for aerobic fitness assessment and reference values for obese adults, obese adults with KOA and healthy individuals are shown in table 1.

Table 1: Reference values of 6MWT for KOA, obese and health subjects.

Study	n	Age (years)	Sample characteristics	6MWT Mean (m)	SD (±)	Speed (m/s)
Hulens et al.(2003)[85]	82	18-65	BMI≤26 kg/ m^2	722	64	2.0
	85	18-65	BMI≥27 kg/ m^2	591	54	1.6
	133	18-65	BMI≥35 kg/ m^2	539	68	1.5
Beriault et al.(2009)[84]	21	40-65	BMI=37±10 kg/ m^2	452	9	1.3
Capodaglio et al (2013)[102]	227	20-60	BMI=43±5 kg/ m^2	564	62	1.6
Miller et al (2006)[87]	87	≥60	KOA; BMI≥30 kg/ m^2	442	8	1.2
Messier et al (2013)[103]	150	≥55	KOA;BMI=33±5kg/ m^2	480	15	1.3
Wang et al (2011)[104]	84	≥55	KOA	331	9	0.9
Kennedy et al.(2005)[105]	150	50-73	KOA	412	123	1.1
Kervio et al.(2003)[106]	12	60-70	aparently healthy	545	21	1.5
Jones et al. (1998)[107]	861	60-64	aparently healthy	639	88	1.8
	1566	65-69	aparently healthy	600	102	1.7
	1813	70-74	aparently healthy	580	100	1.6
Troosters et al. (1999)[108]	51	50-85	aparently healthy	631	93	1.8
Camarri et al.(2005)[109]	33	55-75	aparently healthy	659	62	1.8
Carvalho et al.(2008)[110]	32	65-71	aparently healthy	515	28	1.4

- Lower limb strength training: Muscles constantly interact with the synovial joints, and this can influence the osteoarthritis process. The main goal of recommended strength training is to maintain basic muscle functions (movement, joint stability, the absorption of mechanical shock and proprioception[111], avoiding muscle weakness, improving body stability, and posture and body weight support). In addition to being considered essential for the performance of daily activities[100], strength training has a positive effect on the prevention of lower limb injury, one of the KOA risk factors[93]. Weakness of the quadriceps is a frequent occurrence in KOA and previous clinical trials have shown that quadriceps strength training is effective for the improvement of pain and physical fitness[94, 95]. Obesity combined with sarcopenia, termed sarcopenic obesity, is also closely associated with the prevalence of KOA[75]. Intensive strength training can change thigh composition and has shown promise in treating the underlying biomechanical (knee-joint loading) and inflammatory disease pathways[112]. However, in cases of varus malalignment, its effects on pain and on the external Knee Adduction Moment (KAM) have been questionable[96]. In response to this and based on biomechanical analyses, recent approaches suggest that the strengthening of hip abductor muscles can reduce medial knee loading[97]. Reference values for knee strength in adults with KOA are cited in table 2.

Table 2: Reference of main published articles of knee strength and KOA.

Article Authors	Year	Strength Protocol	N Age (years±SD)	BMI±SD (Kg/m²)	Results
Sanchez-Ramirez et al.[113]	2013	Isokinetic extension (60º/s)	N=284 (62±8)	29±5	Ext:0.8±0.4 Nm/kg
Bennell et al.[114]	2013	Isometric extension	N=82 (62±7)	30±4	Ext:1.44 ±0.4Nm/kg
Diracoglu et al.[115]	2009	Isokinetic extension (60º/s) flexion(60º/s)	N=51 (56±10)	24±5	Ext:114±40 Nm Flex:49±18 Nm
Malas et al.[116]	2013	Isokinetic extension (60º/s) flexion(60º/s)	N=61 (59±7)	-	Ext:80±33 Nm Flex:72.2 Nm
Glass [117]	2013	Isokinetic extension (60º/s)	N=2404 F:(63±8) M:(62±8)	31±6	F: 67±25 Nm M:122±52 Nm
Kean et al.[118]	2010	Isokinetic extension (60º/s) Isometric extension	N=20 (54± 9)	30±4	1.43±0.5Nm/Kg 1.81±0.8 Nm
Lim et al.[119]	2009	Isometric extension	N=184 (65±8)	29±5	1.33±0.5 Nm/kg
White et al.[120]	2012	Isokinetic extension(60º/s)	N=1788 (67±8)	<25 25-<30 30-<35 ≥35	1.17±0.4 Nm/kg 1.1±0.4 Nm/kg 1.0±0.4 Nm/kg 0.82±0.3 Nm/kg
Lund et al.[121]	2008	Isokinetic extension (60º/s) flexion (60º/s)	N=79 (≥50)	Normal	Ext:71±26 Nm Flex: 35±14 Nm
Trans et al.[122]	2009	Isokinetic extension (60º/s) flexion(60º/s) Isometric extension flexion	N=52 (60±10)	29±6	Ext:58.5±21 Nm Flex: 39.5±12 Nm Ext: 70±24 Nm Flex: 37±13 Nm

- Flexibility: Patients with symptomatic KOA have poorer flexibility in both the affected and unaffected leg[83], mainly in the hamstrings muscles[123]. Inclusion of stretching exercises is recommended in every exercise training program for adults[100] and can improve the range of motion and physical function in individuals with KOA[90].

- Gait training: In addition to being considered an aerobic exercise, walking is one of the most important functionalities of the human being and is essential for autonomy and an independent life[83]. Functional limitations imposed by KOA symptoms and by obesity cause obese individuals with KOA to employ different gait patterns to find better balance and avoid pain. Hulens and his team (2003)[85] suggest that knee pain is an important predictor of the 6MWT in obese individuals, based on their observation that the distance walked by this group in the study was significantly inferior to lean individuals (table 1). A correct walking pattern could generate some difficulty and joint discomfort during practice, therefore, a multicomponent training has increasingly been suggested. In addition to strength, flexibility and aerobic components of training, gait training should be considered[98].

- Stability and posture training: KOA includes symptoms of instability[99]. Recent evidence has suggested that changes in lower limb biomechanical factors during weight bearing activities may have substantial impact on the ability to maintain a neutral spine posture while moving the extremities in a manner that is independent of the trunk. Stability and posture training is therefore imperative for proper movement and function in all daily activities.

- Weight reduction (in cases of obesity): The OARSI recommendations[12] for weight loss in the treatment of KOA are gaining increasing importance [79-82]. For a general weight loss program, the ACSM guidelines[100] recommend a reduction of 5-10% of initial weight over 3-6 months by an intervention of moderate to intense aerobic exercise, resistance-training and behavior intervention. In cases of KOA, Messier and coworkers (2005)[80] reported that a weight reduction of 1 kg was associated with a knee load reduction of 4 units per step, a clinically meaningful reduction when considered over the many steps performed each day.

- Education: This intervention should include general information for a healthy lifestyle and specific information about KOA, its implications and alternatives for managing and living with it. Likewise, posture strategies and gentle movements can help in pain control. The routine of pain self-assessment is essential for understanding its response to exercise and for management of exercise intensity. The essence of an educational program should be to help patients learn to live with the disease while improving their quality of life and reaching a feeling of wellness [13, 15, 124].

- Psychological approach: Factors such as fear, anxiety, and depression have adverse effects on the disability in people with KOA[69, 73, 92], and like pain, depression is considered a major obstacle for KOA management[69, 89]. An individual's perception of pain severity can be influenced by centrally mediated factors and behavioral components[125]. A structured exercise group class can be an effective way to increase motivation by providing a social support for exercise adherence and, thereby, promoting lifestyle changes[100]. In addition, exercise and physical activity improve factors related to psychological distress and these changes could lead to improved pain and function in people with KOA.

2.3.1. Aquatic Exercise

Aquatic exercise (AE) is an exercise modality that is a group of exercises performed in the water, mainly in the vertical position. AE has been used for rehabilitation (hydrotherapy)[126-130], for athletic training[131-135] and for general fitness[136-141]. According the Aquatic Exercise Association[142], AE can be practiced in shallow or deep water pools and, for both, can be performed with or without music and with or without accessory equipment. In general, positive effects of AE have been reported for aerobic fitness[143-146], strength[147-150], flexibility[151-153]; body composition[154-156], balance[149, 157-161], functional capacity for daily living activities[153, 162, 163], relief of symptoms in some musculoskeletal disorders[127, 164], quality of life[165], and psychological factors such as depression, state of anxiety, and self-esteem[166].

The main characteristics of AE are the utilization of the hydrostatic and hydrodynamics properties of water. The specific properties of water such as hydrostatic pressure, buoyancy and the hydrodynamic resistance are factors that explain the reported chronic adaptations associated with AE programs[167, 168].

AE has become popular as a modality for improving cardiorespiratory fitness while avoiding excessive joint loading[167, 169]. There are some AE programs that are used worldwide and recognized by international aquatic exercise associations[170, 171], including Jogging (JO), Cross Country Ski (SK), Jumping Jacks (JJ), Kicks (KC), Rocking Horse (RH), Water Walking (WW), Alternating Leg Curl (LC) and Twist (TW). Most AE classes, which are not physiotherapy, use music to provide motivation, exercise rhythm and acceleration to help reach the desired intensity. The guidelines of the Aquatic Exercise Association (AEA)[171] recommend that aerobic aquatic exercise classes be performed in water between 28-30º C so as not to compromise the endocrine responses. Water temperatures above 32º C are recommended for passive work, relaxation techniques or for individuals with low movement levels, but are not advisable temperatures for aerobic or strength based exercise[172]. In cases of patients with low aquatic abilities, the Arthritis Foundation Guidelines suggest a superior limit range of water temperature of 31º C[170].

According to AEA guidelines, beyond the variation in music cadence, exercises in water can be performed in three different cadences (land tempo, water tempo and half-water tempo), and this should be considered when planning research protocols[171]. Barbosa and coworkers.[173] studied the effect of music cadence on heart rate (HR) and lactate when performing the “rocking horse” in water tempo and found a significant correlation between HR and music cadence (r=0.61; p<.01) and between lactate and music cadence (r=0.54; p<.01), providing important information for instructors who intend to use music during classes. Alberton and coworkers[134] studied the water running exercise in comparison with maximal land tests and found greater cardiorespiratory responses with increases in music cadence at land tempo AE. With respect to cardiorespiratory training, Raffaelli and coworkers[169] compared cardiorespiratory responses across several AE programs and they concluded that the Alternated Front Kick had higher VO^2 and calorie expenditure than Side Kick, Jogging and Jumping Jacks, when performed at the same music cadences.

With respect to biomechanics it’s well known that buoyancy force is responsible for softening the impact of vertical movements by reducing the vertical ground reaction forces (V-GRF), which are lower in water than on land for the same exercise[140, 174-176]. Therefore, buoyancy is considered the main mechanism for reduction of the intra-articular compression forces in AE[177, 178]. The magnitude of the impact generated by the V-GRF forces will depend on the body immersion level, the body buoyancy of the practitioner and the technical standards chosen[167, 178, 179]. In addition, some exercises are made easier, even with muscle weakness, when performed toward the surface of the pool (and are thus assisted by buoyancy force), while others are made harder when performed toward the pool bottom (and are thus resisted by buoyancy force)[180].

With respect to the main AE programs, studies reveal that stationary exercises performed with vertical propulsion of the body have a greater impact than those obtained in exercises with horizontal displacement of the body, such as water walking[174]. Moreover, they show that, among stationary movements, Cross Country Ski had a lower V-GRF peak than alternated Front Kicks and Water Running[174]. The authors of this study explained that, due to the buoyancy and drag forces created by the contralateral movement, it is possible to reach high intensities without an increase in V-GRF, mainly because of the absence of heel strike and the accentuated propulsive support phase in maximal velocities[175, 181]. With respect to the V-GRF, another study assessed mechanical loading from body weight by using plantar pressures and found, for the same water depth and exercise cadence, that the alternated Knee Lift provided higher impact than Cross Country Ski, and that Cross Country Ski had a higher impact than Jumping Jacks[179].

Concerning neuromuscular aspects, an important difference between AE and land exercise is that, in AE, joints are surrounded by water, thus providing multiplanar movements that allow agonist and antagonist muscles to work in the same movement. For example, the neuromuscular function of the quadriceps and hamstring muscles, acting as agonists and antagonists in the repeated knee flexion-extension exercises, was modified by the flowing properties of water, where an early reduction of agonist activity occurred concurrently with a high level of activity of the antagonists while the level of antagonistic activity was low throughout the range of motion[182]. On the other hand, these same authors suggested that, in a single trial exercise, the level of agonist activity was higher during the final phase of the range of motion when compared with the repeated exercises.

2.3.2. Aquatic Exercise an KOA

Considering the aquatic exercises characteristics and the exercise components suggested in the present dissertation to be included in all KOA intervention programs (cardiorespiratory training[15, 91, 92], strength training[93-97], flexibility training[83, 90], gait training[83, 98], posture and balance training[99],patient education[13, 15] and psychological approaches)[73, 92], the analyses of literature previously published (Table 3) indicates that aquatic exercise, when correctly structured, can be a very complete and embracing exercise type for KOA[168, 171, 183]. Another important aspect of aquatic exercise is that a person in pain has difficulty with weight bearing exercises, and due to buoyancy, aquatic exercise allows aerobic and resistance exercise to be accomplished with less joint overload[151].

Table 3: Reference of main published articles of exercise for KOA.

Article		Sample			Intervention			Assessments
Authors	**year**	**N**	**Age** (years)	**BMI** (Kg/m²)	Type	Days	weeks	
Bennel et al. [114]	2013	82	≥50	29.6 (4)	LE		12	Gait analysis, Pain ,WOMAC, strength
Foley et al.[184]	2003	105	71±9	25-28	AE/LE	3	6	Isometric Quadriceps strength; WOMAC;SF-12
Gill et al. [185]	2009	82	70±9	31±5	AE/LE	2	6	Pain;WOMAC;SF-36
Hinman et al.[165]	2007	71	≥50	33±6	AE	2	6	WOMAC;PASE;6MWT;Step test; Strength
Kim at al.[183]	2012	70	≥60	25-28	AE	3	12	Self- efficacy, body weight Depression, pain and blood lipid level
Lim et al. [186]	2010	75	≥50	≥25	AE/LE	3	8	BPI;SF-36; Strength WOMAC; Body fat
Lund et al. [121]	2008	79	≥50	25-28	AE/LE	2	8	Pain ;KOOS; Balance; Strength
Messier et al. [187]	2009	450	≥55	28-40.5	LE /Diet/ Education	3	72	WOMAC,;6MWT, QOL (SF36),Gait analysis; Strength; Self-image; Mental Health
Schlenk et al. [88]	2011	26	63±10	33±6	LE	6	24	WOMAC;6MWT;Short Physical Performance Battery
Silva et al. [188]	2008	30	>50	25-28	AE/LE	3	18	WOMAC, pain,50 ft
Suomi et al.[148]	2003	64	60-79		AE/LE	2	8	Functional fitness, ADLs and strength
Wang et al.[104]	2011	84	≥55	25-28	AE/LE	3	12	ROM; 6MWT; KOOS
Wyatt et al. [189]	2001	46	45-70		AE/LE	3	6	ROM, thigh girth, pain , 1-mile walk
Thorstensson et al[190]	2005	61	56±6	29±5	LE	2	6	KOOS;SF36

Abbreviations: AE= Aquatic exercise; LE= Land exercise; 6MWT= Six Minutes Walking Test; WOMAC=; Western Ontario and McMaster Universities Osteoarthritis Index; BPI=Brief Pain Inventory; KOOS= Knee injury and Osteoarthritis Outcome Score; ROM= Knee range of motion.

Several studies have examined the effects of water exercise (hydrotherapy, aquatic exercise) on KOA outcomes[104, 121, 139, 151, 153, 157, 161, 165, 183-186, 188, 189, 191-194], mainly on symptoms, functional capacity, knee strength and quality of life. However, there is no consistency among most of these aquatic exercise studies[101, 195, 196] regarding sample characteristics and methodology used, such as exercise quality and volume, intensity management, water temperature, water depth and cueing strategies used[101, 195, 196]. The present literature review indicates that the best results for aquatic exercise programs were obtained in trials longer than 11 weeks, or at least with a total of 24 sessions. However, many studies used protocols shorter than this.

The primary articles on land or aquatic exercise for KOA, that involved samples similar to the present dissertation study or had detailed methodologies that were considered relevant, are referenced in table 3.

Lim and coworkers[186] and Wang and coworkers[104] compared land and aquatic exercise and provided detailed information about exercise protocols. Regarding sample characteristics, the majority of KOA studies have worked with age groups above 55 years old and elderly groups, and with normal weight to obesity grade 1. There are few study protocols focusing on obese adults with KOA. However, Hinman and coworkers[165] studied the effect of aquatic exercise on KOA symptoms and physical fitness of obese adults with KOA, and despite their use of a twice weekly program that lasted only 6 weeks, they had significant improvements. In the study of Kim and coworkers[183], a solid exercise methodology was presented that used music for motivation and the basic aquatic exercise patterns were applied according the AEA guidelines[171]. Although the study of Messier[187] only applied a land protocol, the detailed methodology, the sample size, and the sample characteristics were similar to those of this dissertation study and they included a strong educational component.

Based on this literature review, it is clear that there is a need to develop and validate detailed and controlled exercise protocols for obese adults with KOA symptoms, with the intent to disrupt the KOA/Obesity cycles. Thus, specific goals for the PICO aquatic exercise program were established and methodologies were designed.

Chapter 3: Aims of the study

This chapter presents the general and specific aims stipulated for this dissertation .

3.1 Aims of the study

This study is based on the premise that every person beginning an exercise program for fitness improvement should go through a screening for symptoms of musculoskeletal disorders, mainly KOA, and in cases where symptoms occur, a specific intervention for its management should precede the regular fitness programs, if possible.

The need to improve non-pharmacological interventions for individuals with KOA is obvious, and aquatic exercise is an option for obese patients because it minimizes joint load. Although water exercise is frequently encouraged, relatively little research has been conducted in this area compared to land-based exercise.

The present study aimed, as its main goal, to design and implement an aquatic exercise program specific for improvement of KOA symptoms, physical fitness and health-related quality of life in overweight and obese adults with KOA. In addition, the construction and validation of the Knee OA Pre-Screening questionnaire (KOPS) (Appendix 3) was conducted. Although this was not a part of the primary aim of this study, it was considered important for solving methodological problems relating to the recruitment of patients for further interventions and reducing x-ray costs. This process was very important because it involved a thorough review of the literature about KOA, its risk factors, symptoms and its epidemiology.

We believe that the PICO aquatic exercise could help a person learn how to live with their disease, control pain and other symptoms, and change their outlook about KOA. The feeling of having control over their symptoms could trigger a series of positive changes, including physical function improvements and lifestyle changes, and could ultimately help prevent KOA progression.

Knowing that participants performed the tests to the best of their ability and with maximal effort, and that they were truthful in all self-reported answers, the following specific goals were defined:

1. To design and implement an aquatic exercise program based on the Arthritis Foundation/YMCA Aquatic Program and with the methodological contribution of the Aquatic Exercise Association (AEA).

2. To investigate the effects of the PICO aquatic exercise program on knee pain and other KOA symptoms of overweight and obese individuals;

3. To investigate the effects of the PICO aquatic exercise program on physical fitness (aerobic, strength, flexibility and physical function) of overweight and obese individuals with KOA;

4. To investigate the effects of the PICO aquatic exercise program on KOA health-related quality of life, specifically on the capacity to perform activities of daily living, sports and recreation and on mental health;

5. To investigate the aquatic exercise effect on body composition; although the aquatic program has been designed specifically for KOA symptoms, health-related quality of life and physical fitness, we intended to investigate potential effects on body composition in individuals;

6. To understand how KOA symptoms and physical fitness are associated in overweight and obese individuals;

7. To investigate the KOA symptoms, physical fitness and quality of life outcomes according to body mass index groups;

8. To investigate the factors that affect walking capacity in overweight and obese adults with KOA;

9. To perform the lower limb contralateral analyses to investigate the existence of differences in knee strength, body composition and body morphology, between the most painful knee and the least painful knee.

Chapter 4: Methods

This chapter includes the methodology used in the present study, already published (Appendix 12).Clinical Trial Registration: NCT01832545 .

Yazigi F, Espanha M, Vieira F, Messier SP, Monteiro C, Veloso AP: The PICO project: aquatic exercise for knee osteoarthritis in overweight and obese individuals. *BMC Musculoskelet Disord* 2013, 14:320.

4.1 Study Design

During the literature review and in the development process for sample recruitment, was felt the need to use a tool to help in the pre-screening of individuals who were more likely to have KOA in order to carry out the X-ray examination.

Due the fact of there are few questionnaires published in the literature related to KOA screening, although the major subject of this dissertation is about exercise intervention, the development of the Knee OA Pre Screening Questionnaire (KOPS) (Appendix 4) was done in parallel of the main study (Fig.3). Additionally, details of KOPS construction and validation process can be consulted in the appendix 13 (article under review).

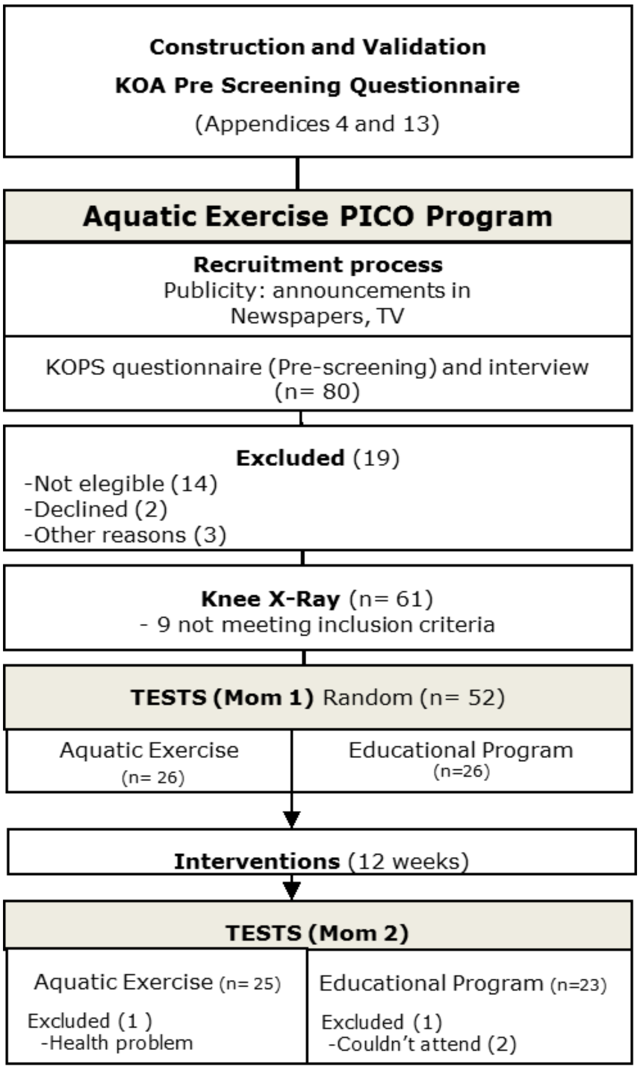


Fig. 3. PICO project fluxogram.

PICO was a single-blinded, randomized controlled trial with a duration of 3 months, 12 weeks. Participants were randomly assigned to one of two groups: aquatic exercise (AE) group and control group (CG) and assessed in two moments. The researchers and personnel responsible for data collection were blinded to the group classes. The study protocol was approved by the Ethical Committee of the Faculdade de Motricidade Humana, Universidade de Lisboa. All of the participants were informed about the procedures and potential risks of the trial, and informed consent was obtained from each subject (Appendix 2).

4.1.1. Sample

Considering the calculation of the sample size, the studies of Messier in 2009[197] and Wang in 2007[151] were used as references because they had a sample with similar characteristics and studied similar outcomes. Both studies showed that a reduction of symptoms in patients with KOA led to a significant improvement ($\alpha<0.05$) of the primary outcome measure, the self-reported physical function. To find an analogous improvement of self-reported physical function of approximately 25%, between the baseline and final measurements in patients with KOA, the minimum number of required patients for the main outcomes was 20. The requirement number of 20 patients was based on a power (1-B) of 0.80 and a significance level of 5% (two-sided). When a dropout rate of 20% is taken into account, at least 25 participants were required to be involved at study onset.

Final sample at baseline included 52 individuals randomized in two groups, as illustrated in fig 3. From 80 volunteers, 61were forwarded to X-ray where 52 fulfilled the clinical and radiological ACR criteria.

Eligibility

Participants in this study were community-dwelling adults from the Lisbon area, volunteers that fulfilled the following inclusion criteria:

(a) age between 40 and 65 years;
(b) BMI≥ 28.0 Kg/m^2;
(c) knee pain;
(d) Clinical and radiographic KOA (unilateral or bilateral KOA grade I-III, tibiofemoral OA or tibiofemoral plus patellofemoral OA);
(e) a sedentary lifestyle (defined as not participating in a program that incorporates

more than 30 minutes per week of formal or supervised exercise;

(f) independent mobility;

(g) and reading and writing knowledge.

The exclusion criteria for subjects were:

- hip or knee replacement or knee surgery within the 6 months prior to the study;
- knee injections within the past 3 months.
- unstable medical conditions;
- skin diseases.

4.1.2. Trial conduct

The recruitment and selection process was performed according to the aforesaid eligibility criteria. To avoid convenience sampling, different strategies were created for advertising and publicizing the PICO project, namely, social networks, television interviews, newspapers and the collaboration of entities/companies made up the main channels for PICO announcements.

All eligible individuals who contacted the study secretariat went through the same selection process, namely, a telephone-based pre–selection stage followed by a face to face interview and completion of the screening questionnaire - KOPS (Appendix 4), which supplied information about demographics, symptoms, signs and risk factors for KOA occurrence. Volunteers who, after completing the questionnaire, fulfilled the ACR criteria for clinical diagnosis[199] received a request for an x-ray examination. The exams were referred to a rheumatologist who made the final diagnosis according to ACR clinical and radiological criteria. If KOA diagnosis was confirmed, the subject was invited to a further interview for a detailed explanation of the project and familiarization with the places for performing the tests as well with the instruments to be used.

4.2 Intervention Programs

During intervention phase, two free of charge programs were established, the Aquatic Exercise Program and Educational Program (PESO comunitário).

4.2.1. Aquatic Exercise (AE)

The aquatic program was based on the guidelines of OARSI and EULAR for KOA management[12, 16], on the Aquatic Exercise Association Guidelines (AEA)[171], on the Arthritis Foundation Aquatics Program instructor's manual[170], on the ACSM's Guidelines for Exercise Prescription[100] and on the analysis of protocols from previous studies [104, 151, 186, 187, 192, 194, 196].

The aquatic program was organized into 24 sessions which were distributed over 12 consecutive weeks, with a frequency of twice a week (table 4). The duration of each session was 60 minutes, as 10 minutes were allotted for patient reception, blood pressure control, pain registry and educational talks; the effective time inside the water was 45 minutes. The indoor pool area had an air temperature of approximately 27±1ºC and a controlled water temperature of 30.5±0.5ºC.

The strategies for production of a high quality aquatic exercise intervention were structured according to AEA guidelines[171] and included overload assessment and management, impact level control (1, 2 or 3)[171], exercise cadence control and appropriate music selection according to exercise goals. In addition to the use of varied and pre-defined cool-down sessions each week, a strong motivational component and pain assessment were anticipated to have an impact in this protocol.

To meet the aims of the study related to KOA management, quality of life and fitness improvements, the AE protocol had specific goals that were organized by sessions according table 4. The primary goals included cardiorespiratory training, strength training, joint mobilization and gait training. The secondary goals were aquatic adaptation, flexibility, stability training, socialization and mental health.

All sessions followed the same structures design. Warm up was structured based on the combination of recruitment of large muscles groups with travelling movements (walking patterns) and with main joints mobilization, in static position.

Considering the cardiorespiratory component, in first 3-4 weeks this component was worked out mainly by the exploration of different walking patterns in combination with upper limb movements. Posteriorly, basic aquatic aerobic exercise patterns were introduced. Exercise cadence, changes in the movement direction and its trajectory, acceleration and arm levers were used to vary the exercise intensity. The individual aerobic training zone was calculated for each participant by Karvonen formula and, the

Rate of Perceived Exertion Borg CR10, adapted Borg Scale (0-10), was used for control aerobic target zone, according to guidelines for exercise intensity management[100]. Also, heart rate monitors were used every class to guarantee the desired intensity zone and to help participants acquire consciousness of exercise intensity. Aerobic exercises was worked with an alternative method to the continuous training method, where the heart rate is worked out within the minimum and maximum range of the heart rate target zone, and it sets were performed in intercalary way with resistance strength sets. As schematized in table 4, the cardiorespiratory component was introduced by small bouts of duration and low intensity, being progressively increased.

The intensity of strengthening exercises was controlled by the Omni - Perceived Exertion Scale for Resistance Exercise (OMNI-RES) and the specific strength exercises were performed to recruit the following muscle groups: quadriceps, hamstrings; hip adductors/abductors, gluteous, abdominals, erector spinae, quadratus lumborum, latíssimus dorsil, pectoralis, trapezius, biceps and triceps. The aquatic strength exercises used can be consulted in the appendix 3. Workouts were organized to have a progressive overload every two weeks. Water was the main instrument that created resistance in the exercises and only in the last weeks, progressively and according to the level of progression of the participants additional equipment was added in the upper limbs, to increase the water resistance and consequently, the exercise overload.

Another aspect that was considered was the level of aquatic ability of each participant. Exercises such as underwater breathing and flotation were used in small doses to reduce fear of the water and to ensure that participants were comfortable moving around the pool (Table 4). This component not had a pre-defined duration, was worked gradually from 15 to 15 days, interleaved with other session components, always in transition phases between the parts of the session. During the exercises for aquatic adaptation skills, the music was turned off to ensure that would not compromise the purpose of the task.

Concerning music used, based on literature review, a cadence of 128 beats per minute (BPM) was chosen for the firsts four weeks, allowing better range of motion with low segment acceleration. The following weeks the BPM changed to 132, requiring greater effort, particularly in the body stabilization and in the capacity to maintain the range of motion, increasing segment speed, applying power against water resistance.

Table 4: The aquatic exercise protocol design for the 12 weeks of PICO program.

Week		Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9	Week 10	Week 11	Week 12
Music BPM		128	128	128	128	128	132	132	132	132	132	132	132
Warm up (5-8')	Duration	8'	8'	8'	8'	8'	8'	5'	5'	5'	5'	5'	5'
	Exercise Pattern	Walking Patterns (Forward, backward and side-to side; power walk) combined with static and gentle movements of main joints- Use hands to keep thermal confort											
Aquatic Adaptation	Exercise type	Vertical balance and travellings		Submersion and undewater breathing		Ventral flotation	Dorsal flotation	Transition from horizontal to vertical position		Transition from horizontal to vertical position		No	
Cardio (15-30')	Duration	3X 5'	4X 5'	4X 5'	(1x10') + (2 x 5')	(1x10') + (2 x 5')	(1 X 15') +(1 x 5')	1X15' + (2 x 5')	1X15' + (2 x 5')	(1X15') + 10'	(1X15') + 10'	(1 X 20') + (1x 5')	(1 X 20') + (1x 5')
	Exercise pattern	Walking patterns with variation of upper limb patterns			10' walking patterns +(2x5´) of basic aquatic patterns(Jumping jack, Ski, Leg Curl and Kicks)	10' Basic Patterns+ 2X5'walking	15' walking + 5´of basic patterns(jumping jack, Ski, Leg Curl and Kicks)	15' basic patterns +2x5´walking	15' basic patterns +2x5´walking	15' basic patterns +10´walking	15' walking+10'basic patterns	20' mixed (walk+basic patterns)+ 5' walking	20' mixed (walk+basic patterns)+ 5' walking
	Intensity (%HRmax and Borg scale)	57%-67% RPE 4-6	57%-67% RPE 4-6	57%-67% RPE 4-6	64-74% RPE 5-6	64-74% RPE 5-6	60-80% RPE 5-7	60-80% RPE 5-7	60-84% RPE 5-8	64-84% RPE 6-8	64-84% RPE 6-8	74-84% RPE 7-8	74-84% RPE 7-8
	Impact Level	1	1	1	1	1 and 2	1 and 2	1, 2 and 3	1,2 and 3	1, 2 and 3	1, 2 and 3	1, 2 and 3	1, 2 and 3
Strength (10-15')	Repetitions	2x 8	1 x16	2x16	$2x16^{t1} + 1x8^{tt}$	2x16(T1)+1x8 (Land Tempo)	2x16(T1)+1x8 (Land Tempo)	1x24T1 + 1x8tt	1x24T1 + 1x8tt	2x24	2x24	3x16	3x16
	Sets interval	Active 1-2'	Active 1-2'	Active 1-2'	Active 1-2'	Active 1'	Active 45'''	Active 45''	Active 1'	Active 30''	Active 30''	Active 1-2'	Active 1-2'
	Equipment added	NO	NO	NO	NO	NO	NO	NO	NO	Drag (gloves)	Drag (Gloves)	Drag (gloves)	Drag (Gloves)
	Intensity (Omni Scale)	6-7	6-7	6-7	6-7	6-8	6-8	6-8	6-8	7-8	7-8	7-8	7-8
	Cadence	t1 = water tempo	t1 = water tempo	t1 = water tempo	t1= water tempo tt= land tempo	t1 and tt	t1 and tt	t1 and tt	t1 and tt	t1 and $t^{1/2}$ = (water half tempo)	t1 and $t^{1/2}$	2x t1 and 1x tt	2x t1 and 1xtt
Final Part (5-6')		Static Stretching on the wall	Static Stretching (center)	Dinamic/stactic streching	Dance+ Dinamic/stactic	Dinamic/stactic	Dinamic/stactic	Dinamic/stactic on the wall	Dance+ stactic streching	Dinamic/ stactic	Dinamic/stactic on the wall	Dinamic/stactic	Dance dinamic stretching

Educational themes were also addressed during the classes. One educational theme per week was reinforced, such as: *What did you have for breakfast? Let's try, during this week, to improve the quality of our breakfast. Next class I will check what you ate; remember that you should assess yourself about knee pain, let's try to learn how to live with it.*

Maximizing adherence is a key element dictating success of any exercise intervention. Beyond the adherence enhancement that, in general, supervised sessions can provide, the exercise instructors used the following behavioral techniques:

- encouraged social contact between participants;
- promoted frequent contact during all intervention phases;
- defined clear behavioral goals and allowed feedback on achievements;
- helped participants self-monitor their pain and exercise intensity to complete activity;
- and established personal commitment to the project through the exercise leader.

4.2.2. Educational program: Control Group (CG)

The control group was not enrolled in any exercise program but participated in the educational program “PESO comunitário”. This program is based on appropriate clinical guidelines and on validated behavior change principles[200]. Implemented by an intervention team with expertise gained from current scientific research in weight control determinants, this program was open access to all interested adults who wished to manage their weight and health. It has operated since 2005 with the objectives of preventing obesity or reducing excess weight as well as some of the risk factors for adult obesity, through a change toward steady healthy habits, attitudes and behaviors. PESO lasted three months and comprised 12 sessions, each one with one hour and a half duration, on a weekly basis.

4.3 Knee osteoarthritis: screening and diagnosis

The Knee Osteoarthritis Pre-Screening questionnaire (KOPS) (Appendix 4) was validated by the authors and considered useful for this purpose (Appendix 13). KOPS addresses physical function, activity level, co-morbid diseases, KOA risk factors and symptoms, height and weight (to determine BMI) and caregiver status. The demographic data that were collected included data on occupation, income, and educational level. The medical form was used to determine co-morbidities and to analyze any self-reported information on medications. The overall KOPS score has acceptable to good reliability with a Cronbach's Alpha of 0.747 and satisfactory internal consistency with an Intraclass Coefficient (ICC) for average measures of 0.646. The results for a test-retest of one-week interval for each component ranged from 0.895 to 0.992 for ICC and from 0.894 to 0.979 for Cronbach's Alpha (Appendix 13).

OA diagnosis and severity classification:

To confirm OA and classify its severity, the same X-ray protocol was used for all subjects. Bilateral, anterior-posterior, weight-bearing knee radiographs were used to identify OA in the tibiofemoral joint, and sunrise views were used to identify OA in the patellofemoral compartment. The severity of tibiofemoral OA was measured using the Kellgreen and Lawrence grading scale [201].

4.3.1. Outcomes and instruments

The main outcomes were KOA symptoms (pain and other symptoms), quality of life and physical fitness (aerobic capacity, strength and flexibility). The secondary outcomes were body composition, lower limb morphology and lifestyle.

Pain was assessed by KOOS pain, BPI and NRS, others KOA symptoms by KOOS symptoms; physical fitness by 6MWT, FRSTST,CSR; isokinetic and isometric knee strength and handgrip tests; health and quality of life by ADL, Sport/rec and QOL KOOS' dimensions and by BDI. Body composition was assessed by BMI and by DXA scanner; morphology by waist, thigh and knee circumferences; lifestyle was assessed by IPAQ, WALI and PGICS questionnaires.

During the study, all participants were allowed to maintain their usual medications, including analgesics and NSAIDs. A detailed record of medication was completed at baseline and at the 3 months post-intervention testing.

With the exception of screening tests, all tests were performed by all subjects at baseline and three months later, at the end of the exercise intervention, using the same protocols and were evaluated by the PICO team member(s). The tests and questionnaires were distributed over two nonconsecutive days, taking into account the fatigue levels of the subjects and the necessary avoidance of overload. Therefore, the knee strength test and the Six Minute Walking Test were conducted on different days (see appendix 1).

KOA symptoms and Health Quality of Life

- Knee Injury and Osteoarthritis Outcome Score (KOOS). This questionnaire included five dimensions to measure KOA-specific health-related quality of life (QOL), knee pain (Pain), other disease-specific symptoms (O.Symptoms), activities of daily living (ADL), and sport/recreation function (Sport/Rec). A score in each dimension was calculated as the sum of the items included and was then converted to a 0-100 scale, with 0 representing extreme knee problems and 100 representing no knee problems. The KOOS is validated for patients with knee injury or with KOA and is a reliable and responsive self-administered instrument for short-term follow-up[202]. The Portuguese validation has acceptable reliability with Cronbach's alpha coefficients between 0.77 and 0.95 and ICC ranging from 0.82 to 0.94 for the KOOS subscales[203] (Appendix 5).

- Brief Pain Inventory (BPI) – short version. A consensus panel, the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT), recommended the inclusion of the short version of Brief Pain Inventory (BPI) in all trials that intend to assess chronic pain[204]. BPI is widely used, and it is a reliable, valid instrument that assesses pain by its history, location, intensity and interference with daily activities in individuals with osteoarthritis[205]. The both dimensions of BPI short-form were used (Pain severity and the Pain interference) using a 24 hours recall period. The Portuguese version of this assessment was validated, and recent studies have provided strong support for its reliability and validity[206, 207] (Appendix 6).

- Numerical Rating Scale (NRS). The subjects learned to self-assess their knee intensity pain via the 0-10 point NRS[208]. The NRS was used to assess pain intensity before and after the aquatic exercise class and whenever it was necessary.

- Beck Depression Inventory (BDI-II). This instrument, developed by Beck and colleagues[209], includes 21 items used to rate the severity of depression according to the clinical definition. It is one of the most popular and widely used instruments for assessing the severity of depressive symptomatology. The Portuguese version[210] shows a good internal consistency, a factor structure very similar to the original version [209, 211], and an adequate convergent validity (Appendix 7).

Physical fitness

- Six Minutes Walking Test (6MWT). The distance (d) and gait speed (v) of the 6MWT are used to assess the aerobic capacity and the walking ability of the patient. The test was performed individually and according to the *American Thoracic Society protocol* (ATS)[212], in a controlled indoor environment that was 46 meters in length and rectangular in shape. The 6MWT is a highly reproducible assessment in obese individuals (r=0.926; 95% CI 0.816-0.972, *p*<.001) [84], and it has been used in studies with KOA[88, 101, 187, 213-215].

- Chair Sit and Reach test (CSR). The CSR test is a safe and socially acceptable alternative to traditional floor sit-and-reach tests and is a reasonably accurate and stable measure of hamstring flexibility[107]. The subjects were allowed three attempts for each limb, and the best of these scores was recorded to the nearest centimeter.

- The Back Scratch Test (BS). The BS is a measure of overall shoulder range of motion that involves measuring the distance between (or overlap of) the middle fingers behind the back with a ruler [216]. After a familiarization trial, this test was assessed twice, alternately with both hands, and the best value of each measurement was recorded.

- Five-Repetition Sit-To-Stand Test (FRSTST). This test is a widely used measure of functional strength. The ICC values for the test demonstrate good-to-high test-retest reliability for adults and subjects with osteoarthritis [88, 217, 218].

- Knee Strength. A dynamometer Biodex System III (Biodex Medical Inc., Shirley, NY, U.S.A.) was used for the isokinetic assessment of knee strength (flexor and extensor muscles) and isometric knee strength, bilaterally. The less painful leg was tested first. Gravity correction to torque was calculated at 45 degrees (0=straight leg). The range of motion for testing was pre-determined from 20º to 80º for all subjects. Extreme ranges of knee motion were excluded from testing as they are known to be painful and frequently non-executable by this patient population, e.g., full extension due to quadriceps weakness. Similar procedures, according to the dynamometer used, have been adopted in other surveys involving the same population[219-224].

Prior to measurement, the subjects were seated on the dynamometer with their knee and hip joints at 90º. Crossover shoulder, belly and knee straps, as well as a lap belt were used to restrain the subjects' movements. The lever arm pad was strapped around the lower leg, two centimeters above the lateral malleolus of the fibula. The axis of rotation of the dynamometer was aligned with knee joint's axis of rotation. Joint warm-up consisted of gentle free movements of flexion and extension of the knee.

Maximal Isokinetic Strength was measured on a concentric/concentric mode, at an angular velocity of 60º/s. Among the low velocity groups, the 60º/s velocity has been used in other studies and provided better stability for this population[225]. The subjects performed one set with minimum overload for habituation and two sets of three repetitions with a 120-second rest between sets. The subjects were oriented to perform the test by exerting maximum pressure on the isokinetic arm through the entire range of movement. Vigorous verbal encouragement was given to each subject during the test. The set with the highest extension peak torque and with the lowest coefficient of variation was chosen for analysis.

The angle of best torque of the knee extension, obtained from each subject in the isokinetic test, was chosen for the isometric test. The maximal knee extension isometric test was applied in one set of three repetitions during five seconds, with a 30 second relaxation interval between repetitions. The best of the three force-time curves was chosen according to the highest peak.

Mean quadriceps and hamstring muscle strength per leg was calculated (Nm) and divided by patient's weight (Kg).This measure (in Nm/Kg) has an excellent intra-rater reliability (intraclass correlation coefficient=0.93) in patients with KOA [118]. Traditional hamstring-to-quadriceps (H:Q) was calculated (Isokinetic flexor peak torque/ Isokinetic extension peak torque), as well the bilateral strength deficit for flexors and extensors [(Isok. peak torque$_{_LPK}$ less Isok peak torque$_{_MPK)}$*100/Isok. peak torque$_{_LPK}$)]. Strength test-retest reliability for 6 participants tested twice in our lab, 6–8 days apart, had an ICC of 0.92.

- The Handgrip Strength Test (HST). This test evaluates maximal isometric force of the muscles of the hand and forearm. Although the sample of this study did not have hand OA, this test has been used in obese individuals as an indicator of total body strength and functionality[226, 227]. The adopted protocol for this project is the same as the protocol that was used for Portuguese adults in the national observatory [228]. Prior to the test, the grip dynamometer was adjusted to the size of the hand of each subject. Subjects were to stand with their arms along the body, without contact with the trunk, and with their elbows slightly bent at 20º. Testing was first conducted on the dominant hand followed by the non-dominant hand. The force was to be performed during the expiratory phase and a valsalva maneuver was to be avoided. After three trials, if the difference between each value was within 3 kg, the test was considered complete. If a larger difference was observed, then the test was repeated after a sufficient rest time. The best repetition was chosen for further analysis.

Body Composition and Lower Limb Morphology

- Body composition. Body composition was assessed by DXA, BMI and waist-to-hip ratio. A DXA scanner (QDR 4500A, fan-beam densitometer, software version 8.21; Hologic, Waltham, USA) was used to measure whole body, trunk and lower limb fat mass (FM%). DXA measures the attenuation of X-rays pulsed between 70 and 140 kV synchronously with the line frequency for each pixel of the scanned image. According to the protocol described by the manufacturer, a step phantom with six fields of acrylic and aluminum of varying thickness and known absorptive properties was scanned alongside each subject to serve as an external standard for the analysis of different tissue components. The same technician positioned the subjects, performed the scans and executed the analysis using the standard analysis protocol. Based on test-retest using 10 subjects, the coefficient of variation (CV) in PICO staff for FM was 2.6%, and the total error of measurement (TEM) 0.02 kg.

  Body mass index was calculated as mass (measured in kilograms by a standard calibrated scale) divided by height squared (measured in meters, with a stadiometer (Seca, Hamburg, Germany). Waist-to-hip ratio was calculated dividing the waist circumference by the hip circumference. Stature, body mass, waist, hip and thigh circumferences were collected by a certified anthropometrist based on procedures established by ISAK[229] and the knee circunference according Lohman[230]. The intra-observer technical error for circumferences and diameters measures in the pilot study ranged from 0.3.

Lifestyle

- International Physical Activity Questionnaire (IPAQ). The short form of IPAQ was chosen because it is easy to apply. Despite its reliability having been verified in many countries and with different populations[231-233], some studies have indicated that the IPAQ-SF typically overestimates physical activity[234]. However, this instrument was used for controlling the amount of physical activity along the study and not for any classification of physical activity level. All participants received an introductory explanation about how to complete the questionnaire, and their answers were confirmed during the interviews. Data were processed according to IPAQ guidelines[235] (Appendix 8).
- The Weight and Lifestyle Inventory (WALI). The WALI is designed to obtain demographics information, weight and dieting histories, eating and exercise habits, and relationships with family and friends[74]. The Portuguese version (IPEV) and its translation process is published in a national book[200]. PICO project used only the sections G, K and Q of the Portuguese version (IPEV) for controlling alcohol and tobacco consumption, dietary patterns and clinical historic (Appendix 9).
- Perception of change: Patient Global Impression of Change Scale (PGICS) is very commonly used in clinical research, particularly in the musculoskeletal area[236]. Dichotomous classification was used for the perception of change (5-7=yes, had significant changes; 1-4=did not have significant changes), according to the original article (Appendix 10).

4.3.2. Statistical analysis

Descriptive statistics, including frequencies for categorical variables, means with standard deviations (SD) for continuous variables was used. Normal distribution of continuous variables were tested by Kolmogorov-Smirnov test. Correlation between continuous variables at baseline was analyzed using Pearson correlation coefficient (r) interpreted as strong ($r \geq 0.7$), moderate ($0.5<r<0.7$) and weak ($0.3<r<0.5$), and the coefficient of determination was used to interpret r and was obtained by squaring the correlation coefficient r (r^2)[237].

In addition, a contralateral analysis at baseline were performed, where the comparisons between the most painful knee and the Least Painful Knee were done by paired T-tests.

The differences in mean change (baseline minus post-intervention) were compared between groups using the analysis of covariance, adjusted for baseline values of the outcome. Comparisons of changes between groups (CG and AEG) were performed as primary analysis by Univariate analyses of covariance (ANCOVA) where dependent variables were adjusted for baseline pain, gender, BMI, and baseline values. Changes in body mass index were adjusted for sex, baseline values, and for changes in lifestyle (IPAQ and WALLY questionnaires). Mean differences within groups were calculate as Mom1 (baseline) minus Mom2 (after intervention program). Effect size was verified by partial eta squared.

Complementary analyses was performed with baseline outcomes to provide a better understanding about the behavior of KOA symptoms, health-related quality of life and physical fitness in overweight and obese individuals with KOA. Firstly, outcomes organized by BMI groups where mean, standard deviation for KOA symptoms, quality of life and physical fitness was calculated and Kruskal Wallis test was used to compare mean differences of dependent variables (KOOS, BPI, BDI, IPAQ ,6MWD, CSR, HS, FRSTST, knee strength PkTQ) and non-parametric Post Hoc test using Dunn-Bonferroni test for multiple comparisons among BMI group. In the second complementary analyses, stepwise linear regression analyses were performed to understand the potential predictors that could improve the explanation of the variability of the 6MWT in overweight and obese individuals with KOA. Regarding the underlying model assumptions, the independence of predictors and the normality and homoscedasticity were assessed. In a first step the candidate predictors were selected, i.e., the variables with higher association or correlation with 6MWT and less correlated between themselves. The set of candidate predictors comprised the variables sex, age, KOOS O.Symptoms, BPI pain severity, BDI score, FRSTST, isokinetic extension PKTQ, BMI, waist-to-hip ratio and lower limb fat mass. In cases of occurrence of bilateral KOA, measures of the most painful knee (MPK) were used for statistical analyses. The stepwise method was used for the variable selection purpose, considering the criterion Probability of *F*-to-enter ≤.05 and Probability of *F*-to-remove>=.10.

Considering that sometimes professionals do not have access to advanced or expensive resources, three predictive models were proposed. The first was the one obtained from the stepwise method applied to all candidate predictors mentioned in the paragraph above. The second was the model reached when the stepwise method was employed to a subset of the candidate predictors resulting from the exclusion of variables related with the expensive resources (Biodex dynamometer and DXA scanner), i.e., excluding the fat mass and the isokinetic strength outcomes. The third model was the one attained when the stepwise method was performed on a subset of predictors easier to obtain in clinical situations (sex, questionnaires outcomes and waist-to-hip ratio), i.e., considering the previous a subset of predictors excluding FRSTST.

Statistical analysis was performed using IBM SPSS Statistics 20.0 and MedCalc Statistical Software (MedCalc Software, Mariakerke, Belgium). Statistical significance was set at $p<.05$ (2- tailed) for all analyses.

Chapter 5: Results

This chapter are organized by baseline results, including a sample characterization, by the effectiveness of aquatic exercise and by complementary analyses.

5.1 Baseline results

Initially 52 individuals were randomized into two groups, three were excluded from the CG (one due to health reasons and two who could not attempt the assessments in Mom2) and only one participant was excluded from AEG due to health reasons (Fig. 3). The final sample included 48 participants who completed the program and performed all tests. Demographic characteristics for the final sample and for each group are presented in table 5.

Table 5. Frequency analyses of demographic variables at baseline for Control Group (CG), Aquatic Exercise group (AEG) and for total sample.

	Variables	CG (n=23) n (%)	AEG (n=25) n (%)	Total (N=48) n (%)
Sex	Female	17 (74)	18 (72)	35 (73)
	Male	6 (26)	7 (28)	13 (27)
Age Groups (years)	40-49	5 (22)	5 (20)	10 (21)
	50-59	10 (43)	14 (56)	24 (50)
	60-65	8 (35)	6 (24)	14 (29)
Educational Level	Elementary School	5 (22)	1 (4)	6 (12)
	High school grade 9-12	2 (8)	5 (20)	7 (15)
	High school graduated	6 (26)	7 (28)	13 (27)
	College or more	10 (44)	12 (48)	22 (46)
BMI Classification	Overweight	2 (9)	5 (20)	7 (15)
	Obesity grade 1	12 (52)	10 (40)	22 (45)
	Obesity grade 2	6 (26)	6 (24)	12 (25)
	Obesity grade 3	3 (13)	4 (16)	7 (15)
KOA	Unilateral	5 (21)	4 (16)	9 (19)
	Bilateral	18 (78)	21 (84)	39 (81)
Most Painful Knee	Right	12 (48)	15 (65)	27 (56)
	Left	13 (52)	8 (35)	21 (44)
BDI Classification	Low (no depression)	14 (61)	19 (76)	33(69)
	Slight	4 (17)	3 (12)	7(15)
	Moderate	5 (22)	0 (0)	5(10)
	Severe	0 (0)	3 (12)	3 (6)

Abbreviations: BMI=Body Mass Index; BDI= Beck Depression Inventory.

The majority of participants were within the age interval of 50-59 years. Across all participants, the mean age was 55±7 years, the mean weight was 90.8±13.9 kg, the mean height was 161±10 cm and BMI was 35.0± 4.9 kg/m^2. All participants had tibiofemoral KOA diagnosis, and the majority had bilateral KOA. For each participant, knees were classified as most painful knee (MPK) or least painful knee (LPK) according to the pain intensity level (Table 5).

Although the inclusion criteria included the minimum educational level needed to read and write, 88% of participants had more than an elementary school education and 46% had a college education or higher. Regarding the psychological status of participants, 31% of individuals reported depressive symptoms.

Means +/- standard deviations (SD) and Confidence Interval (CI) of all outcomes at Mom1 are shown in Table 6. Independent t-tests revealed no significant differences between groups at baseline, indicating that the randomization process was successful.

The KOOS dimensions with poorest scores were Sport/rec and QOL. At baseline, the means of the BPI results, measured over the previous 24 hours, were below 5 on a 0-10 scale in each dimension, where the Pain Severity dimension registered a mean score for the worst pain of 4.5±2.5, for the least pain of 2.6±2.3, and the mean pain on the testing day was 2.9±2.1. Among the seven items of Pain Interference dimension, the lowest scores were found for walking ability (3.9±3.0) and normal working (3.9±2.5).

An evaluation of depression across all participants revealed a large range of BDI scores. The CI for entire sample was set between minimal and mild depression classification (Table 5 and 6). Only 3 participants of the total sample presented severe depression, and although all of them were in the CG, this was not enough to increase the mean scores in this group when compared with AEG.

The absolute values of knee strength, corresponding to the relative results reported in table 6, were 86±34 Nm (PkTQ ext_{MPK}) and 105±41 (PkTQ ext_{LPK}) for knee isokinetic extension, and 48±22 Nm (PkTQ $flex_{MPK}$) and 54±22 Nm (PkTQ $flex_{LPK}$) for knee isokinetic flexion. The absolute values for isometric knee extension strength were 131±47 Nm (MPK) and 154±58 Nm (LPK).

The mean waist–to-hip ratio across all participants was greater than 0.90 (Table 6), classifying the sample as abdominal obesity, according to the World Health Organization[100]. With respect to BMI, the total fat mass and the trunk fat mass, as well as the mean results and CI reinforced the obesity classification of the majority of participants in this study (Tables 5 and 6).

With respect to the initial level of physical activity, although the weekly mean of physical activity reported by the total sample was classified as a moderate level, none of the individuals were participating in any structured or supervised exercise program and some participants indicated not having any type of physical activity equal to or greater than 10 min (low level). The reported sitting time per week corresponded to a mean of 5.4 hours per day, and some participants reported being in a seated position up to 10 hours per day.

Table 6. Descriptive analyses for outcomes of total sample at baseline.

		CG (N=23)	AEG (N=25)	Total (N=48)	
	(N=48)	Mean (SD)	Mean (SD)	Mean (SD)	95% CI
KOOS	Pain	50.2(20)	45.3(12)	47.7(16.5)	[42.9,52.5]
	O.Symptoms	55.5(23)	46.6(17)	50.7(20.6)	[44.7,56.7]
	Sport/rec	33.0(22)	26.0(15)	29.4(18.9)	[23.9,34.8]
	ADL	58.2(24)	49.9(16)	53.9(20.5)	[47.9,59.8]
	QOL	38.6(19)	33.8(19.3)	36.1(19.0)	[30.6,41.6]
BPI	Severity	3.7(1.9)	3.4(2.0)	3.6(1.9)	[3.0,4.1]
	Interference	3.6(2.2)	2.9(2.4)	3.3(2.3)	[2.6,3.9]
BDI	Depression score	12.3(7.7)	11.5(11.3)	11.9(9.7)	[9.0,14.7]
Physical function	6MWT (m)	552 (78)	546 (86)	549(81)	[525,573]
	FRSTST(s)	10.8 (3.0)	11.2 (2.0)	11.0(2.7)	[10.2,11.7]
	Handgrip test (Kg)	29.7 (9.0)	29.5 (10.0)	29.6(9.8)	[26.7,32.4]
	CSR_{MPK} (cm)	-5.1 (11.0)	-7.4 (11.0)	-6.3(10.7)	[-9.4,-3.2]
	BST right (cm)	-8.4 (9.0)	1.2(3.0)	-9.3(9.2)	[-12.0;-6.6]
Knee Strength	Isom $PkTQ_{MPK}$ (Nm/Kg)	1.34 (0.5)	1.50(0.4)	1.44(0.5)	[1.30,1.58]
	Isom $PkTQ_{LPK}$ (Nm/Kg)	1.64 (0.6)	1.70(0.5)	1.68(0.5)	[1.53,1.83]
	Isok PkTQ ext_{MPK} (Nm/Kg)	0.90(0.4)	0.98 (0.3)	0.94(0.3)	[0.84,1.04]
	Isok PkTQ ext_{LPK} (Nm/Kg)	1.15 (0.4)	1.16(0.4)	1.15(0.4)	[1.04,1.26]
	Isok PkTQ $flex_{MPK}$ (Nm/Kg)	0.49 (0.3)	0.55(0.2)	0.52(0.2)	[0.46,0.59]
	Isok PkTQ $flex_{LPK}$ (NmKg)	0.58 (0.3)	0.61(0.2)	0.60(0.2)	[0.53,0.66]
	Isok H:Q ratio $_{MPK}$ (%)	0.54(0.2)	0.59 (0.2)	0.57(0.2)	[0.51,0.62]
	Isok H:Q ratio $_{LPK}$ (%)	0.49(0.1)	0.54(0.1)	0.52(0.2)	[0.48,0.56]
	BL Deficit Isom ext (%)	17.2(17)	9.2(20)	13.1(18)	[7.3,18.8]
	BL Deficit Isok ext (%)	19.0(26)	13.4(21)	16.1(24)	[9.3,23.0]
	BL Deficit Isok flex (%)	10.4(31)	9.1(17)	9.7(24)	[2.6,16.8]
Body composition	Weight (Kg)	92.7(16.4)	89.1(11.0)	90.8(13.9)	[86.8,94.9]
	BMI (Kg/m^2)	35.2(5.3)	34.8(4.8)	35(5.0)	[33.6,36.4]
	Waist-to-Hip Ratio	0.91(0.1)	0.88(0.1)	0.9(0.1)	[0.87,0.92]
	Total Fat Mass (%)	40.0(8.0)	39.4(7.8)	34.3(10)	[37.4,42.1]
	Trunk Fat Mass (%)	40.5(7.0)	39.3(6.7)	39.9(6.8)	[37.9,41.9]
IPAQ	Physical activity (MET/week)	959(808)	796(610)	871(714)	[664,1078]
	Sitting time (min/week)	2080(766)	2350(889)	2258(808)	[2023,2492]

Abbreviations: KOOS= Knee injury and Osteoarthritis Outcome Score BPI= Brief Pain Inventory; BDI= Beck Depression Inventory; Test; 6MWT=Six Minutes Walking Test; FRSTST= Five Repetitions Sit to Stand Test; CSR= Chair Sit and Reach; BST=Back Scratch Test; MPK= Most Painful Knee; LPK=Least Painful Knee; Isom= Isometric; PkTQ= Peak Torque; Ext= Extension; Flex= Flexion; H:Q= Hamstrings:Quadriceps; BL= Bilateral Deficit; BMI= Body Mass Index; FM= Fat mass; IPAQ= International Physical Activity Questionnaire.

5.1.1. Correlations between KOA symptoms, quality of life and physical fitness outcomes

This subsection provides important information about how the physical fitness outcomes are associated with KOA symptoms and health-related quality of life. The Pearson correlation coefficients between self-reported questionnaires (KOOS; BDI and BPI) and physical tests at Mom1 are shown table 7. (With respect to KOOS dimensions, is important to note that the score nearest to zero represents the worst condition).

Among the physical tests, the FRSTST, the CSRT and the BST did not show any correlation with KOOS, BDI and BPI (Table 7). On the other hand, the 6MWT had a significant, positive correlation with all self-reported outcomes, with exception of the KOOS Sports/rec dimension. Additionally, the HST was significantly correlated with all questionnaires with the exception of the KOOS Pain and KOOS Sport/rec. Regarding pain, both 6MWT and HST, had a strong negative correlation with BPI severity and a moderate and weak, respectively, positive correlation with KOOS Pain. Additionally, the 6MWT and HST showed a strong negative correlation with mental health assessed by BDI.

Pearson coefficients for knee strength tests (Table 7) showed that all three knee strength tests were not correlated with KOOS Pain, KOOS Sport/rec or KOOS QOL. However, there was a moderate, positive correlation with KOOS O.Symptoms and a weak, positive correlation with KOOS ADL for both extension strength tests and a strong, positive correlation for isokinetic knee flexion test. Additionally, the mental health evaluation showed a negative correlation with the isometric and isokinetic tests, having a moderate relationship with the isometric PkTQext and the isokinetic PkTQflex and a weak relationship with the isokinetic PkTQext.

Regarding body composition, moderate to strong correlations were found for fat mass with both BPI dimensions, BDI and KOOS ADL; only the KOOS Sport/rec dimension showed no correlation with fat mass. The lower limb fat mass was significantly correlated with all self-reported outcomes, with the exception of the KOOS Sport/rec, as mentioned above. BMI showed only a weak, positive correlation with BDI and a moderate, positive correlation with BPI severity.

Table 7. Correlation analysis between physical fitness and KOA symptoms and quality of life outcomes.

Outcomes	KOOS					BDI	BPI	
N=48	Pain	O.Symptoms	ADL	Sport/rec	QOL		Sev	Int
6MWT	.352*	.528***	.452**	.175	.358*	-.435**	-.625***	-.524***
HST	.261	.340*	.478**	.187	.315*	.471**	-.451**	-.454**
FRSTST	-.111	-.113	-.102	.103	-.153	.223	.128	.085
CSRT$_{MPK}$	-.146	.013	-.038	-.077	-.216	.081	-.023	.271
BST	-.058	.194	-.105	-.229	.014	-0.58	-.238	-.033
Isom PkTQ$_{MPK}$	.133	.305*	.275*	.154	.244	-.392**	-.210	-.238
Isok PkTQ ext$_{MPK}$	.126	.336*	.292*	.222	.204	-.287*	-.258	-.205
Isok PkTQ flex$_{MPK}$	.092	.313*	.442**	.087	.088	-.310*	-.479**	-.399**
BMI	-.191	-.250	-.115	-.028	-.216	.294*	.359*	.279
Waist/Hip Ratio	.292*	.188	.167	.104	.322*	-.298*	-.205	-.279*
Total FM	-.234	-.327*	-.400**	-.116	-.282	.496***	.385**	.462**
Trunk FM	-.171	-.270	-.377**	-.070	-.187	.422**	.355*	.418**
Lower limb FM$_{MPK}$	-.326*	-.410**	-.413**	-.160	-.320**	.448**	.405**	.460***

Abbreviations: 6MWT=Six Minutes Walking Test; HST=Handgrip Strength Test FRSTST= Five Repetitions Sit to Stand Test; CSR= Chair Sit and Reach; BST= Back Scratch Test; MPK= Most Painful Knee; LPK= Least painful Knee; BMI= Body Mass Index; FM= Fat Mass; KOOS= Knee Injury and Osteoarthritis Outcomes Scoress;BDI= Beck Depression Inventory; BPI=Brief Pain Inventory; Sev=Severity, Int=Interference.

**p*<.05, ***p*<.01, ****p* <.001.

Additional correlative analyses were conducted across physical tests and self-reported outcomes. The highest correlations were found between 6MWT and HST (r=.770; *p*<.001), HST and FRSTST (r=-.343; *p*<.05), and FRSTST and 6MWT (r=-.387; *p*<.01). In addition, BDI scores were significantly correlated with BPI interference scores (r=.423; *p*<.01) and with the knee related quality of life of KOOS (r=-.292; *p*<.05), while all KOOS dimensions (where 100 represents the healthy status) were negative and significantly associated with both BPI dimensions (*p* <.01).

5.1.2. Lower limb contralateral analysis: comparison between the most and least painful knee

Comparisons of knee strength, lower limb morphology and body composition were done between the MPK and LPK and are expressed in the table 8 .The dominant lower limb for all sample was the left leg, being that 44% of participants reported the left knee as the most painful knee.

Table 8. Contralateral analyses of most painful and Least Painful Knee at baseline T-tests for limb comparisons.

		Most Painful Knee			Least Painful Knee		Mean Difference		
		N	Mean	SD	Mean	SD	Mean	SD	*p*-value
Knee Strength	Isok PkTQ ext (Nm)	48	85.8	34.0	105.3	41.5	19.5	24.4	<.001***
	Isok PkTQ flex (Nm)	48	47.6	22.1	54.3	22.5	7.1	12.2	<.001***
	Isom PKTQ ext (Nm)	48	130.6	46.6	153.8	57.9	23.2	32.9	<.001***
	Ratio H:Q	48	56.1	20.0	51.1	13.4	-55.0	18.6	.065
	Total work Isok ext (J)	48	208.7	86.2	259.6	110.2	50.8	62.4	.001**
	Total work Isok flex (J)	48	134.5	72.2	156.8	74.5	22.3	39.0	.001**
Body Composition and morphology	Thigh circumference (cm)	35	51.8	22.6	61.3	6.8	9.6	22.1	.015*
	Knee circumference (cm)	37	37.2	18.8	46.1	5.1	9.1	18.2	.007**
	Lower limb FM (%)	47	40.1	10.1	40.2	10.3	0.1	2.5	.558

Abbreviations: Isom= Isometric; Isok= Isokinetic PkTQ= Peak Torque; Ext= Extension; Flex= Flexion.; H:Q=Hamstrings:Quadriceps.

*p<0.05, **p<0.01, ***p <0.001.

Regarding strength bilateral deficit (BLD) (table 8),the significant lower PkTQ values found for MPK represents a BLD of -16±23% in the isokinetic extension, -9.7± 24% in the isokinetic flexion and -13.1±19% in the isometric extension.

Differently, the ratio H:Q was 7% higher in the MPK, but no differences were found between limbs. Total work in isokinetic extension and flexion were higher in the LPK, with contralateral differences around 20 and 14% respectively.

With respect to the body composition and morphology, values for the MPK were significantly lower; 16% in the thigh circumference and 20% in the knee circumference, while no significant difference was found for lower limb FM.

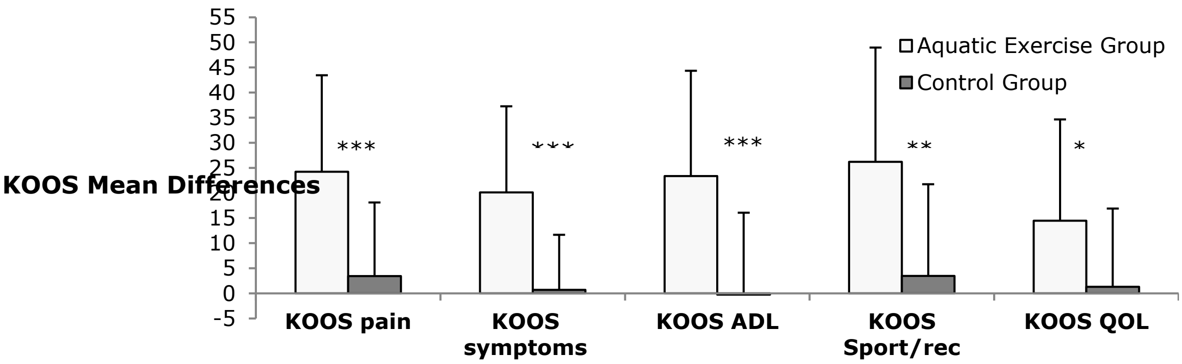
5.2 Effectiveness of Aquatic exercise

The results and discussion about the effects of aquatic exercise in this study were organized and compared by groups (Table 9, Table 10, Fig. 4 and Fig. 5), according to previous randomization: Control Group (CG) and the Aquatic Exercise Group (AEG). Data from questionnaires and physical fitness were presented by outcome type: KOA symptoms and quality of life (KOOS; BPI and BDI) and physical fitness (physical function, knee strength and body composition). Results for lifestyle (IPAQ and WALLY) were presented at the end of the physical fitness item.

The participant adherence in both groups was high with only one participant excluded from AEG, due to health problems, and three from CG, as shown in fig 2. The strategies incorporated into the AE program, including the motivational component and the extra classes offered every 15 days to ensure that all participants fulfilled the 24 sessions, were very effective.

5.2.1 KOA symptoms and quality of life

The mean changes between groups in all dimensions of KOOS were significant different (Fig. 4). Pain-dose response to exercise was analyzed after the three months of intervention, by the interpretation of KOOS pain dimension, related to the past week and by BPI related to last 24 hours. KOOS pain changed in the CG from 50.2±20 to 53.7±19 and from 45.3±12 to 69.6±19 in the AE group.



*$p<0.05$, **$p<0.01$, ***$p<0.001$.

Fig 4. Group effect analysis, mean differences with standard deviation error bars of dimensions of Knee injury and Osteoarthritis Outcome Score (KOOS) for the Aquatic Exercise Group and Control Group.

KOOS O.Symptoms changed in the CG from 55.2±23 to 55.9 ±20 and from 46.6±18 to 66.7±19 in the AEG; KOOS ADL had a slightly decrease from 58.2±24 to 57.9 ±22 in CG while the AEG showed an increase from 49.9±16 to 73.3±19; KOOS Sport/rec changed in the CG from 33.0±22 to 36.5±27 and from 26.0±15 to 52.2±25 in the AEG; KOOS QOL changed in the CG from 38.6±19 to 39.9 ±21 and from 33.8±19 to 48.3±25 in the AEG.

All KOOS dimensions did not reveal significant effect from the covariates BMI and sex. except for the baseline values of Pain, O.Symptoms and ADL dimensions which revealed meaningful group effect (*p*<.01) (Fig. 4).

Table 9 presents ANCOVA analysis for each item of the O.Symptoms and Pain dimensions of KOOS. No group effect was observed in the questions S5-S7 and in the pain frequency (P1) and pain on bending (P4). Significant group effect were found on four items of symptoms, swelling (S1), knee noise (S2), knee hang up (S3) and straighten (S4). Regarding pain items, higher group effect was found for pain on walking (P5) and on up and downstairs activity (P6).

Table 9. Group effect analysis for questions scores of Symptoms (S1-S7) and Pain (P1-P9) dimensions of KOOS questionnaire (0-4 where 4 is the worst condition). ANCOVA adjusted for sex BMI value no baseline.

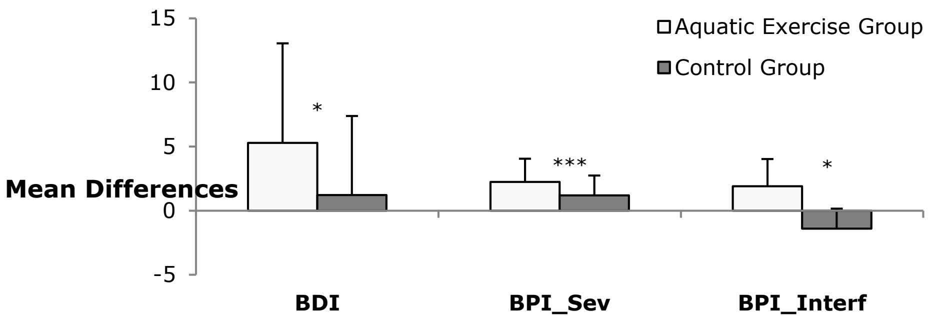
	Control Group			Aquatic Exercise Group			ANCOVA	
	Mom1	**Mom2**	**Changes**$^{\delta}$	**Mom1**	**Mom2**	**Changes**$^{\delta}$	**Group effect**	
	Mean(SD)	Mean(SD)	Mean(SD)	Mean(SD)	Mean(SD)	Mean(SD)	F	*p*-value
S1:Sweelling	1.6(1.4)	1.7(1.2)	-0.1(0.8)	2.0(1.4)	1.3(1.1)	0.7(1.3)	4.75	.035*
S2:Noise	2.0(1.1)	2.0(1.1)	0.0(0.5)	2.7(1.1)	1.9(1.0)	0.8(0.9)	7.01	.011*
S3:Knee Hang up	2.1(1.2)	1.9(0.9)	0.3(1.0)	2.3(0.8)	1.4(0.9)	0.9(0.9)	7.49	.009**
S4:Straighten	0.9(1.0)	1.2(1.1)	-0.3(1.2)	1.4(1.2)	0.8(1.2)	0.6(1.0)	6.23	.016**
S5:Bend	1.5(1.3)	1.6(13)	-0.1(1.0)	1.8(1.3)	1.4(1.6)	0.4(1.4)	2.16	.149
S6:Morning Stiffness	2.0(1.1)	1.7(1.1)	0.3(1.2)	2.3(1.0)	1.3(0.9)	1.0(1.2)	3.52	.068
S7:Position Stiffness	2.2(1.2)	2.0(1.2)	0.2(0.9)	2.4(0.8)	1.6(1.1)	0.8(1.1)	3.37	.073
P1:Frequency	2.9(0.9)	2.7(0.9)	0.2(0.9)	3.0(0.7)	2.3(1.0)	0.7(1.3)	2.87	.097
P2:Twisting	1.9(0.9)	1.9(1.0)	0.0(1.1)	2.4(0.6)	1.4(1.0)	1.0(1.0)	6.41	.015**
P3:Straighten.	1.6(0.9)	1.7(1.0)	-0.1(1.4)	1.9(0.9)	1.0(1.1)	0.9(1.1)	6.88	.012**
P4:Bending	2.0(1.3)	1.8(1.2)	0.2(0.8)	2.3(0.8)	1.5(1.2)	0.8(1.4)	1.97	.168
P5:Walking	1.1(0.8)	1.5(0.9)	-0.4(1.0)	1.6(0.8)	0.6(0.8)	1.0(0.9)	19.07	<.001***
P6:Up/Down	2.3(1.3)	2.2(1.2)	0.1(0.9)	2.8(0.6)	1.5(1.1)	1.3(1.1)	12.49	.001**
P7:At night	1.4(1.0)	1.5(1.1)	-0.1(1.1)	1.8(0.9)	0.8(0.9)	1.0(1.2)	9.72	.003**
P8:Sitting	1.3(0.9)	1.3(1.0)	0.0(0.9)	1.6(0.8)	0.8(0.9)	0.8(1.0)	7.06	.011*
P9:Standing up	1.8(1.0)	1.6(1.1)	0.2(0.7)	2.2(0.8)	1.2(1.2)	1.0(1.2)	5.54	.023*

*p<0.05, **p<0.01, ***p <0.001 $^{\delta}$*negative=worsening; positive=improvement.*

Some items of CG registered worsening condition, while the AEG had improvements in all items: S1(CG=-6%; AEG=35%); S2(CG=0%; AEG=30%);

S3(CG=14%; AEG=39%); S4(CG=-33%; AEG=43%); S5 (CG=-7%; AEG=22%); S6(CG=15%; AEG=43%); S7(CG=9%; AEG=39%); P1(CG=7%; AEG=23%) ; P2(CG=0%; AEG=42%); P3 (CG=-6%; AEG=47%); P4(CG=10%; AEG=35%); P5(CG=-36%; AEG=63%); P6(CG=4%; AEG=46%); P7(CG=-7%; AEG=56%); P8(CG=0%; AEG=50%) and P9(CG=11%; AEG=45%).

Changes in depressive symptoms and pain in the past 24 hours are represented in fig. 5. The BDI scores improved 46% in the AEG (11.5±11 to 6.2±7) and 10% in CG (12.4±8 to 11.1±8), with significant group effect [F (1, 42) = 7.35, p= .010]. No covariate effect was observed. In relation with self-reported pain, both dimensions of BPI had improvement in comparison to the baseline (p<.001), with a significant group effect for Pain Severity (p<.001) and for Pain Interference (p=.010); in the Pain Severity, the CG had a mean change of 32% (from 3.7±2 to 2.5±2) and the AEG had a mean change of 65% (from 3.4±2 to 1.2±1) while in the Pain Interference the CG had a mean change of 39% (from 3.6±2 to 2.2±2) and the AEG had a mean change of 66% (from 2.9±2 to 1.0±1).



*p<0.05, **p<0.01, ***p <0.001.

Fig 5. Group effect analysis, mean differences with standard deviation error bars of the of the Beck Depression Inventory (BDI) and both dimensions of Brief Pain Inventory (BPI): BPI severity and BPI interference for the Aquatic Exercise Group and Control Group.

With respect to the administration of medication for pain control 72% of AEG and 47.8% of CG reported to have taking analgesics or anti-inflammatories in the baseline and, after interventions, the frequency of medicine administration was 52.0% in AEG and 54.5% in CG.

5.2.2 Physical fitness

Physical fitness was assessed by physical function tests and knee strength tests. Means of physical function tests for baseline and after intervention, mean differences within groups, and results of ANCOVA to compare the physical function variables between groups are shown in table 10.

Higher group effect was found in the 6MWT and in the FRSTST, being that the effects of covariates were different in each one; despite baseline effect, BMI was the only covariate with significant effect in the 6MWT [F (1, 42) = 4.093, p=.049] and the the only covariate with significant effect in the FRSTST was pain severity obtained by BPI [F (1, 42) = 4.581, p= .038]. Results of the others three physical function tests didn't have covariates effect.

Table 10 indicates that, excepting for the 6MWT, the CG had some improvements in all others physical function tests, but AEG had better relative results (%): FRSTST(CG=9%; AEG=27%); Handgrip(CG=3%; AEG=14%); CSR_{MPK}(CG=86%; AEG=104%); CSR_{LPK} (CG=89%; AEG=101%) and BST right (CG=14%; AEG=39%).

Table 10. Group effect analysis of the physical function tests, controlling for baseline BPI severity pain, gender, BMI, and baseline values for physical fitness tests (Mom1= Baseline and Mom2=After interventions).

	Control Group (N=23)			Aquatic Exercise Group (N=25)			ANCOVA	
	Mom1	Mom2	Changes	Mom1	Mom2	Mean Dif	Group Effect	
	Mean (SD)	Mean(SD)	Mean dif(SD)	Mean (SD)	Mean (SD)	Mean dif (SD)	F	p -value
6MWT (m)	552 (78)	534 (84)	↓ 18 (42)	546 (86)	601 (92)	↑ 55 (38)	39.4	<.001***
FRSTST (s)	10.8 (3)	9.8 (3)	↓ 1 (2)	11.2 (2)	8.1 (2)	↓ 3.0 (1)	14.8	<.001***
Handgrip (Kg)	29.7 (9)	30.7 (8)	↑ 1.0 (3)	29.5 (10)	33.6(10)	↑ 4.1 (3)	10.1	.003**
CSR $_{MPK}$ (cm)	-5.1 (11)	-0.8 (8)	↑ 4.4 (6)	-7.4 (11)	0.3 (9)	↑ 7.7 (7)	2.4	.032*
CSR $_{LPK}$ (cm)	-4.4 (11)	-0.5 (8)	↑ 3.9 (5)	-8.0 (11)	0.04 (9)	↑ 8.1 (8)	2.5	.124
BST right (cm)	-8.4 (9)	-7.3 (8)	↑ 1.2(3)	-10.2 (9)	-6.1(8)	↑ 4.0(3)	10.8	.002**

Abbreviations: BMI= Body Mass Index; Test; 6MWT=Six Minutes Walking Test; FRSTST= Five Repetitions Sit to Stand Test; CSR= Chair Sit and Reach; LPK= Least Painful Knee; MPK= Most Painful Knee; BST= Back Scratch Test;

*p<0.05, **p<0.01, ***p <0.001

Regarding knee strength results showed in the table 11, significant group effect were found only for Isokinetic peak torque at flexion, for both knees (p<.05). Excepting for the isometric peak torque of MPK, the comparison of the magnitude of changes between groups indicated higher improvements in the AEG in all tests, but not enough to be statically significant Δ $IsokPkTQext_{MPK}$ (CG=9%;AEG=14%); Δ $IsokPkTQext_{LPK}$ (CG=3%;AEG=9%); Δ $IsokPkTQflex_{MPK}$ (CG=20%;AEG=31%);Δ $IsokPkTQflex_{LPK}$ (CG=16%;AEG=26%); Δ $IsomPkTQ_{MPK}$ (CG=22%;AEG=14%) and Δ $IsomPkTQ_{LPK}$ (CG=9%;AEG=18%). Effect size for knee strength tests ranged from small to medium. No group effect were observed for bilateral deficits neither for H:Q ratio for both limbs.

Table 11. Group effect analysis of Isokinetic and Isometric normalized strength tests, controlling for baseline BPI severity pain, gender and baseline values for strength tests.

	Control Group (N=23)			Aquatic Exercise Group (N=25)			ANCOVA	
	Mom1	Mom2	Changes	Mom1	Mom2	Changes	Group ffect	
	Mean (SD)	Mean(SD)	Mean dif(SD)	Mean(SD)	Mean (SD)	Mean dif (SD)	F	p -value
IsokPkTQ ext_{MPK}(N-M/Kg)	0.90(.4)	0.98 (.3)	-0.08(.2)	0.98 (.3)	1.12(.4)	-0.14(.2)	1.08	.305
IsokPkTQ ext_{LPK} (N-M/Kg)	1.15 (.4)	1.19 (.4)	-0.04(.3)	1.16(.4)	1.27 (.4)	-0.11(.2)	1.94	.171
IsokPkTQ $flex_{MPK}$ (N-M/Kg)	0.49 (.3)	0.59 (.2)	-0.10(.1)	0.55(.2)	0.72(.2)	-0.17(.1)	5.96	.019*
IsokPkTQ $flex_{LPK}$ (N-M/Kg	0.58 (.3)	0.67 (.3)	-0.09(.2)	0.61(.2)	0.77(.2)	-0.16(.1)	3.76	.049*
IsomPkTQ $_{MPK}$ (N-M/Kg)	1.34 (.5)	1.64 (.6)	-0.30(.3)	1.50(.4)	1.71(.6)	-0.21(.4)	0.85	.363
IsomPkTQ $_{LPK}$ (N-M/Kg)	1.64 (.6)	1.79 (.6)	-0.15(.4)	1.70(.5)	2.02(.6)	-0.31(.4)	2.91	.085
Isok H:Q ratio $_{MPK}$ (%)	0.54(.2)	0.60 (.2)	-0.06(.2)	0.59 (.2)	0.68(.2)	-0.08(.2)	1.10	.300
Isok H:Q ratio $_{LPK}$ (%)	0.49(.1)	0.56 (.1)	-0.07(.1)	0.54(.1)	0.62(.2)	-0.08(.1)	0.40	.530
BL Deficit Isok ext (%)	19.0(26)	16.0(22)	3.0(21)	13.4(21)	12.2(20)	1.2(18)	0.00	.981
BL Deficit Isok flex (%)	10.4(31)	11.5(20)	-1.1(27)	9.1(17)	4.7(20)	4.4(22)	1.37	.248

Abbreviations: MPK= Most Painful Knee; LPK=Least Painful Knee; Isom= Isometric; PkTQ= Peak Torque; Ext= Extension; Flex= Flexion; H:Q= Hamstrings:Quadriceps; BL= Bilateral Deficit.

*p<0.05, **p<0.01, ***p <0.001

Although weight loss was not a main outcome of this study, the AEG presented at the end of program a body mass reduction of 2% (from 89.1±11 to 87.3±11 Kg) while CG didn't have alteration (from 92.7±16.5 to 92.8 ±16.8 Kg). In the same way, the comparison of BMI changes between groups, controlled for sex, baseline value and lifestyle changes (IPAQ and WALLY) were significant [F (1, 41)=8.343, p=.006], where no group effect from the covariates was observed. The amount of physical activity and sitting time per week were assessed by IPAQ. A significant group effect was revealed in total MET/week (p=.046) being increased from 968.9±800 to 1025.2±896 in the CG and increased from 780.2±626 to 1443.5±1345 in the AEG. In respect to the sitting time per week, no group effect were observed [F (1, 42) = 5.310, p=.214] although some changes was observed (from 2156.5±716 to 2128.7±843 min in the CG and from 2350.4±889 to 1940.4±1089 min in the AEG). The magnitude of improvements in eating patterns was slightly higher in the CG, but no significant group effect was detected [F (1, 42) = 5.310, p=.214].

The Patient Global Impression of Changes assessed in the Mom2 revealed that 20 participants (80%) in the AEG expressed to have changed significantly (scores 5-7) and in the CG, only one participant (4.3%) reported to have changed and the others 22 didn't expressed significant changes (scores 1-4).

Group effect size (ES) in the analysis of covariance was evaluated using Partial Eta Squared (η_p^2) as seen in table 12. The effect size was classified as small (η_p^2<0.06), medium (0.06<= η_p^2<0.14) and large (η_p^2>=0.14)[238].

Table 12. Group effect size from univariate analysis of variance adjusted for sex, BMI, pain and baseline values.

OUTCOMES	Effect Size	(η_p^2)
6MWT	.484	large
FRSTT	.261	large
CSRT $_{MPK}$	.053	small
CSRT $_{LPK}$	.055	small
BST (right)	.205	large
Handgrip	.194	large
Isom PkTQ$_{MPK}$	.021	small
Isom PkTQ$_{LPK}$	.063	medium
Isok PkTQ ext$_{MPK}$	.024	small
Isok PkTQ ext$_{LPK}$	.043	small
Isok PkTQ flex$_{MPK}$	.122	medium
Isok PkTQ flex$_{LPK}$	.100	Medium
KOOS pain	.251	large
KOOS symptom	.287	large
KOOS ADL	.248	large
KOOS QOL	.101	medium
KOOS sport/rec	.218	large
BPI severity	.265	large
BPI interference	.147	large
BDI	.149	large

Abbreviations: 6MWT=Six Minutes Walking Test; HST=Handgrip Strength Test FRSTST= Five Repetitions Sit to Stand Test; CSR= Chair Sit and Reach; BST= Back Scratch Test; MPK= Most Painful Knee; LPK= Least Painful Knee;; BPI=Brief Pain Inventory; Sev=Severity, Int=Interference; BDI= Beck Depression Inventory.

Results showed that there was a large group ES for all physical function tests, except the CSRT which had a small ES. Strength tests had small ES, with exception for isokinetic knee extension of LPK and both Knee flexion tests which had a medium ES. A large group ES was found in four KOOS dimensions (Pain, O.symptoms, ADL and Sport/rec), in both BPI dimension and in BDI. The KOOS QOL has a medium group effect size.

5.3 Complementary analyses

Complementary analyses present the baseline results from another point of view. We intended to provide a better understanding about the behavior of the main outcomes related to body mass index groups according to ACSM classification[100] and also, to identify potential predictors of walking capacity in overweight and obese adults with KOA through a linear regression analysis of the 6MWT.

Although all participants were overweight or obese, the BMI range in our sample encompassed the overweight and three obesity grades (Overweight: 25-29.5; Obesity grade I= 30 - 34.99 Kg/m^2; Obesity grade II= 35 – 39.99 Kg/m^2 and Obesity grade III= ≥40 Kg/m^2). In this way, a complementary analyses was performed to provide some references value related to KOA symptoms, functional fitness and quality of life, according BMI group (overweigh, obesity grades I, II and III) (Tables 13, 14 and 15) and differences were tested by the non-parametric test, Krushal-Wallis and multiple comparisons between groups was performed with non-parametric post hoc analysis using Dunn-Bonferroni test.

Means and standard deviations for KOOS dimensions by BMI classification are reported in the table 13. Only O.Symptoms dimension differed significantly across the groups, (χ^2_{KW} (3)= 8.08, *p*=.044) showing the grade III group a significant poorest condition than grade II (*p*=.011) and overweight group (*p*=.021). The others KOOS dimensions showed the same tendency for obesity grade III, however, the differences were not significant.

Table 13. Means and standard deviations for the five dimensions of KOOS questionnaire according to BMI classification (KOOS score range is 0-100 where nearest to zero is the worst condition).

N=48			KOOS									
			PAIN		**O.SYMPTOMS**		**QOL**		**ADL**		**SPORT/REC**	
BMI Classification		N	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Overweight		7	51.6	13.8	60.3	17.1	38.4	18.9	53.4	15.2	32.9	17.5
Obesity	**grade I**	22	47.1	18.0	48.0	21.5	39.8	17.5	56.9	21.1	28.6	20.4
	grade II	12	53.3	16.8	59.5	19.0	33.8	22.6	53.4	23.5	30.8	18.8
	grade III	7	36.0	7.7	34.7 *	13.8	26.0	17.0	45.6	19.1	25.7	18.6

Abbreviations: KOOS= Knee injury and Osteoarthritis Outcome Score; Symptoms= Other Symptoms; QOL = Quality of Life, ADL =Activities of Daily Living and Sport/rec = Sports and Recreation function; *BMI*= Body Mass Index.

*significant differences from Overweight and Grade II levels (p<.05).

Table 14 shows means and standard deviation of BMI groups for BPI, BDI and IPAQ. The comparisons among this groups by Kruskal Wallis analysis indicated significant differences in the BPI severity (χ^2_{KW} (3) = 8.99, *p=.029)* and in the IPAQ (MET/week), (χ^2_{KW}(3) = 4.62, *p*=.007*)*. No significant differences were found for BPI interference (χ^2_{KW}(3) = 2.60, *p*=.457), although grade III reported higher scores than other group. BPI severity had significant differences between groups grades I and III (*p*=.010) and between grades II and III (*p*=.004). Results for depression, although not being significant (χ^2_{KW}(3) = 7.19, *p*=.066) showed higher scores for participants with obesity grade II and III (BDI= 15.9±13.6 and 14.9±5.6 respectively) and lower scores for the overweight group (BDI= 5.6±5.8).

Regarding physical activity per week, only the overweight group was significantly different when compared with all grades of obesity, specifically with grade I (*p*=.009), with grade II (*p*=.001) and with grade III (*p*=.003) groups. On the opposite, in sitting time no significant differences among groups were found (χ^2_{KW}(3) = 1.73, *p*=.631), but grade III reported highest sitting time per week.

For physical fitness (Table 15), significant differences among BMI groups were observed for 6MWT [χ^2_{KW}=(3)=9.19, *p*=.027] and for the both strength tests: Isokinetic knee extension [χ^2_{KW} =(3)=9.54, *p*=.023] and for isometric knee extension [χ^2_{KW}=(3)=12.77, *p*=.005]. Results for the others physical fitness tests were worst for grade III but not statically significant. Post hoc multiple comparisons between groups showed significant differences for the 6MWT between grade III and all the others groups (overweight group, *p*=.006; grade I, *p*=.010; grade II, *p*=.013). The same trend was observed in the isokinetic knee extension, where significant differences between overweight and all the others were (grade I, (*p*=.010; grade II, *p*=.024; grade III, *p*=.003).

Table 14. Means and standard deviations for Brief Pain Inventory (Severity and Interference), Beck Depression Inventory (BDI) and International Physical Activity Questionnaire (IPAQ), according to BMI classification.

		BPI				**BDI**		**IPAQ**			
		Sev		**Interf**				(MET/week)		**Sit** (Min/week)	
BMI Classification	N	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Overweight	7	3.9	2.0	2.7	2.8	5.6	5.8	1639$^{\beta}$	1244	2053	793
Obesity grade I	22	3.3	1.9	3.1	2.4	10.8	7.3	876	479	2227	827
grade II	12	2.8	1.5	3.1	2.0	15.9	13.6	590	550	2253	885
grade III	7	5.6*	1.4	4.3	2.0	14.9	8.9	566	359	2566	706

Abbreviations: BPI= Brief Pain Inventory; BDI= Beck Depression Inventory; IPAQ= International Physical Activity Questionnaire

*significant difference from Grade I and II (p<.05); $^{\beta}$ significant difference from Grade I ,II and III (p<.05)

Table 15. Means and standard deviations for physical fitness tests, according to BMI classification.

		6MWD (m)		**CSR** (cm)		**Handgrip**		**FRSTS** (s)		**Isom PkTQ** (Nm/Kg)		**Isok PkTQ ext** (Nm/Kg)	
BMI Classification	N	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Overweight	7	586	68	-5.1	10	34.1	10.5	9.8	2.1	2.0	0.3	1.3	0.3
Obesity grade I	22	557	93	-4.1	11	29.9	11.5	10.8	2.7	1.4	0.4	0.9	0.3
grade II	12	557	64	-8.2	11	28.5	8.4	11.2	2.5	1.3	0.5	0.9	0.3
grade III	7	476$^{\delta}$	39	-11.5	6	25.7	1.9	12.1	3.2	1.2	0.4	0.8	0.1

Abbreviations: 6MWT=Six Minutes Walking Test; CSR= Chair Sit and Reach; FRSTST= Five Repetitions Sit to Stand Test; Isom= Isometric; Isok=Isokinetic; PkTQ= Peak Torque; Ext= Extension.

$^{\delta}$ Significant difference from others groups (p<.05).

5.3.3. Predictive factors of 6MWT in overweight and obese adults with KOA

Prior to performing linear regression analyses to identify predictive factors of 6MWT, correlation analyses were conducted to gain a better understanding of how KOA symptoms and quality of life (measured by KOOS; BPI, BDI) and physical fitness outcomes (strength, flexibility and body composition) are associated with the distance walked during a 6MWT. Pearson product-moment correlation coefficients are shown in table 16.

Among KOOS dimensions, only the Sport/Rec showed no significant correlation with 6MWT. Other Symptoms and ADL showed a strong correlation with the 6MWT. Furthermore, BPI pain scores had a stronger correlation with 6MWT than the KOOS Pain dimension.

Table 16. Pearson product-moment correlations and 2-tailed p-value between Six Minutes Walking Test (6MWT) and Knee injury and Osteoarthritis Outcome Score (KOOS), Brief Pain Inventory (BPI), Beck Depression Inventory (BDI), physical function, knee strength, International Physical Activity Questionnaire (IPAQ) and Body Composition

		6MWT	
	Variables	*R Pearson*	*p-value*
KOOS	Pain	.352	.014*
	Symptoms	.528	<.001***
	ADL	.452	.001**
	Sport/Rec	.175	.233
	QOL	.358	.013*
BPI	Pain Severity	-.625	<.001***
	Pain Interference	-.524	<.001***
BDI	Depression	-.435	.002**
Physical Function	Handgrip test	.770	<.001***
	FRSTST	-.387	.007**
	$CSRT_{MPK}$	.018	.902
Strength tests	Isometric PeakTorque $_{MPK}$	.505	<.001***
	Isometric PeakTorque $_{LPK}$	.574	<.001***
	Isokinetic PeakTorque extension $_{MPK}$	.513	<.001***
	Isokinetic PeakTorque extension $_{LPK}$	.542	<.001***
	Isokinetic PeakTorque flexion $_{MPK}$	.655	<.001***
	Isokinetic PeakTorque flexion $_{LPK}$	.572	<.001***
Body composition and morphology	BMI	-.408	.004**
	Waist-to-Hip ratio	.399	.005**
	Total Fat Mass	-.526	<.001***
	Trunk Fat Mass	-.643	<.001***
	Lower limb Fat Mass $_{MPK}$	-.760	<.001***
	Lower limb Fat Mass $_{LPK}$	-.769	<.001***
IPAQ	Physical activity	.179	.223
	Sitting time	-.039	.795

Abbreviations: MPK=Most painful knee ;LPK=Least Painful Knee

p<0.05, **p<0.01, ***p <0.001*

Mental health, represented by BDI, had a significant correlation (p<.001) with the 6MWT. Of the physical function and strength tests, the handgrip test was strongly correlated with the 6MWT while the isokinetic knee extension and flexion and isometric knee extension had a moderate correlation with the 6MWT. With respect to body composition, lower limb fat mass was strongly and inversely correlated with the 6MWT. All other body composition variables had moderate correlations, while the waist-to-hip ratio had a positive correlation. The 6MWT showed no significant correlation with the IPAQ outcome.

Predictors for the 6MWT in obese adults with KOA were found using stepwise linear regression (Table 17). Three models were achieved based on three different sets of candidate predictors, according to the expenditure/cost (availability) of resources needed to collect variables data. The three models can explain more than 60% of the variations in the results.

Table 17. Multiple regression models of predictive factors for 6MWT.

Model	*Adj.* R^2	*F*	Variables	*B*	*SE B*	*β*	*p*
Model 1	.725	41.49					
			Constant	849.68	32.38		<.001***
			%FM_ $_{MPK}$	-4.39	0.73	-.537	<.001***
			BPI pain severity	-17.27	3.58	-.407	<.001***
			FRSTST	-5.61	2.51	-.182	.030*
Model 2	.649	29.99					
			Constant	649.81	36.16		<.001***
			Sex	92.37	18.58	.510	<.001***
			BPI pain severity	-14.05	4.20	-.336	.002**
			FRSTST	-6.88	2.71	-.225	.015*
Model 3	.607	37.26					
			Constant	572.29	20.48		<.001***
			Sex	101.64	19.29	.561	<.001***
			BPI pain severity	-14.16	4.45	-.339	.003**

In the first model (F= 41,485; *p*<.001), the variance in 6MWT was explained. We first considered all candidate predictors (sex, age, KOOS Symptom, BPI pain severity, BDI score, FRSTST, isokinetic extension PKTQ, BMI, waist-to-hip ratio and lower limb fat mass) using stepwise linear regression. The variables that remained significant were the %Fat mass of the most painful knee, BPI pain severity ($BPI_{severity}$) and FRSTST (Table 17). The equation of model 1 is as follows:

Model 1:	6MWT (m) = 849.676 – 4.883 (Lower Limb FM %) -17.270 (BPI Sev) - 5.606(FRSTT)

Once DXA scanner and BIODEX isokinetic dynamometer are some specialized and expensive equipment, a second model was obtaining also through stepwise method without considering the outcomes from the scanner and dynamometer (fat mass and isokinetic strength). The model is significant and the explained variance was .649. (F= 29,989; p<.001) The significant variables were Sex, $BPI_{severity}$ and FRSTST (Table 17). The equation of second model is as follow:

Model 2:	6MWT (m) = 649.797 + 92.367 (Sex) – 14.048 (BPI Sev) – 6.878 (FRSTST), where sex=1, for male and sex=0, for female.

Considering the same candidate predictors as those used in model 2, a third model was tested but without inclusion of the lower limb strength assessed by FRSTST, a physical test that would not be convenient to perform in a clinical context. The third model was also significant (F= 37,262; *p*<.001) and explained 61% of the variance. In this model two variables predicted 6MWT, Sex and $BPI_{severity}$. The equation of this third model is as follow:

Model 3:	6MWT (m) = 572.292+ 101.641(Sex) – 14.162 (BPI Severity), where sex=1, for male and sex=0, for female.

Chapter 6: *Discussion

This chapter presents the discussion according the results organization: baseline, effectiveness of aquatic exercise and complementary analysis.

6.1 Baseline outcomes

A comparison of our results with previous publications is limited because there are few clinical trials with similar inclusion criteria, particularly with regard to the presence of KOA in combination with age and BMI interval.

Among sample characteristics, a relevant factor was the relatively high educational level of a majority of participants, which is very important with regards to test comprehension and the quality of answers in self-reported questionnaires.

The walking distance on the 6MWT at Mom1 of our participants was similar to that reported by Hulens and colleagues [85] for the BMI group≥35Kg/m^2 and higher than that obtained by Beriault and coworkers [84]. The eligibility criteria for the first study, however, did not include KOA and the age range was larger than in our sample. The age interval in the second study was the same as in our sample, however there was no screening for KOA occurrence, although the mean BMI (37 Kg/m^2) most likely implies the existence of obesity-related pathologies, including KOA. The 6MWT reported by the Messier study [103] was lower than our results, however their eligibility criteria included having KOA and the BMI of participants was similar; on the other hand, the mean age of participants in their study was higher than in ours.

Despite the fact that our participants were obese adults with KOA, the 6MWT indicated that their functional capacity with regards to walking ability and aerobic fitness was not compromised. This may be because they were younger in comparison with other studies and were still actively employed and leading an independent life. Furthermore, the confidence interval of KOOS and BPI were low (KOOS Pain CI=42.9, 52.5 and BPI severity CI=3.0, 4.1), as were the scores for depression, and these variables were correlated with 6MWT (Table 7).

The difference between strength values obtained in this study in comparison with other studies may be explained by the age difference as well as by the type of protocol used, namely the arc of motion of the test, speed and type of dynamometer used. The initial knee strength results were compared with other studies (Table 2). The isokinetic knee extension strength of our participants (Table 6) were slightly higher than the ones found by White and coworkers[120]; although participants in this study had a similar BMI, they were, on average, older. In contrast, Kean and coworkers [118] reported higher isokinetic strength for extension (1.43 Nm/Kg) in a sample with similar mean age and similar pain scores (KOOS Pain nearest to 50), although with a lower

BMI (30±4 Kg/m^2). Finally the H:Q ratio of both limbs were slightly lower than the normative value of 60% at an angular velocity of 60º /s[239, 240] suggested in the literature, being higher in the most painful knee (57%) than in the least painful knee (52%) and revealing an imbalance between the quadriceps and hamstring muscles[239, 240].

In the case of isometric knee strength, our results for extension was similar to that reported by Bennel and coworkers[114] and somewhat lower than that reported by Kean and coworkers[118]. Our baseline results for the MPK at flexion shown in Table 8 are in line with results reported by Diracoglu and coworkers[115] and higher than results obtained in other studies (Lund and coworkers.[121]; Trans and coworkers[122]). The study of Malas and coworkers[116] was the only one with better results than ours, however no information about BMI was provided. The reported differences when comparing our results with other studies can be explained by differences in sample BMI, age and KOA symptoms.

6.1.1. Correlations between KOA symptoms, quality of life and physical fitness outcomes

Although correlation coefficients can indicate how variables are associated, the coefficient of determination (r^2) results in a percent value, which makes it easier to interpret associations between the components of physical fitness, KOA outcomes and quality of life in overweight and obese individuals (Table 7).

With regards to physical tests and knee pain, BPI severity dimension (at the moment and related to the last 24 h) had a better association with all physical tests (BPI severity, r^2=39% and BPI interference, r^2=27%) than the KOOS pain dimension (pain in the last week). It is well known that chronic pain intensity can vary greatly over a week and when questionnaires were given on the testing day, our results showed that the pain intensity nearest to the testing day had more influence on test performance. This is a relevant finding indicating that pain assessment should be conducted as near as possible and before to the physical tests in futures studies with KOA. Additionally, self-reported questionnaires that assess pain at the moment and/or in the last 24 h, should be preferably chosen.

The analysis of Pearson coefficient and the coefficient of determination (r^2) confirmed that the 6MWT is still considered a very useful instrument as an indicator of functional status because, beyond its ability to assess walking ability and an essential weight bearing capacity for independent life, it was shown to be directly affected by KOA symptoms, body composition and depressive symptoms, important factors related to health-quality of life. In fact, the only strong correlation found was between the state of depression and 6MWT, showing that attitudes and beliefs can negatively impact the capability of accomplishing this physical task. Additionally, pain had a mostly mechanical pattern, affecting postural control required in walking. Pain, articular swelling, inflammation and structural damage can inhibit muscle activation in individuals with KOA, particularly in the quadriceps muscles, and can contribute to strength deficits and atrophy, increasing joint loading and changing gait velocity[43, 44].

In contrast to pain behavior, the other KOA symptoms manifest a pattern that is more constant throughout the week and are moderately associated with the 6MWT, although the report of KOOS symptoms was related to the past week6M. With the exception of the KOOS sports/rec, 6MWT was significantly correlated with KOOS O.Symptoms (r^2=28%), KOOS ADL (r^2=20%), KOOS QOL (r^2=13%) and BDI (r^2=19%).

The handgrip strength test, which might be considered a reliable test of functional status and quality of life in obese and overweigh adults with KOA, was significantly correlated with KOOS O.Symptoms (r^2=12%), KOOS ADL (r^2=23%), KOOS QOL (r^2=10%), BDI (r^2=22%), BPI intensity (r^2=20%) and BPI interference (r^2=21%).

Regarding the relationship between knee strength and KOA pain and other symptoms, results showed that neither isokinetic nor isometric knee extension strength were correlated with any pain intensity scores (BPI severity and KOOS pain), and only isokinetic knee flexion had a significant association with BPI severity, accounting for 16% of its variability. On the other hand, KOOS other symptoms were significantly correlated with all knee strength tests, but accounted for only 9-11% of variability.

Our study is one of the few that considers how psychological status affects performance on knee strength tests. Our correlation analyses (Table 7) show that all knee strength tests were inversely and significantly correlated with depressive symptoms, with a better explanation of BDI variability found for isometric extension (15%) than for isokinetic flexion of the most painful knee (10%). These results could be due to the fact that both tests involve movements and/or contraction types that are unusual in everyday life activities, requiring greater focused attention and body control than knee extension movement.

With respect to the relationship between body composition and pain intensity (KOOS pain and BPI severity), while no significant association was found between pain and BMI, a positive and significant correlation between pain and fat mass was found, where BPI severity could explain 13-16% of the variability of fat mass (total, trunk and lower limb fat mass) and KOOS pain could explain 11% of the variability in the lower limb fat mass. These results are consistent with the literature[67;65] and could be explained by systemic inflammation, attributed to the adipose tissue, which can contribute to the disability and lower the individual's pain threshold associated with KOA.

Considering the KOA-obesity cycle (Fig. 2), significant correlations were found between BPI interference and KOOS ADL dimension and all fat mass outcomes (r^2 ranged from 14-21%), indicating that KOA pain affects daily living activities and contributes to obesity or, conversely, that obesity increases pain and affects daily living activities.

Regarding depressive symptoms and body composition, the results shown in table 7 are in accordance with previously published reports[69, 71] where variations in the BDI score were positively correlated with fat mass, explaining 25% of variation in total body fat mass, 18% of variation in trunk fat mass and 20% of variation in lower limb fat mass. On the other hand, BDI score only correlated weakly with BMI and waist-to-hip ratio, explaining only 9% of variation.

6.1.2. Lower limb contralateral analysis: comparison between the most and least painful knee

Muscular strength is an important component for physical activity and for the performance of daily living activities. A generally observed phenomenon is that the capacity to generate maximum strength is compromised when the homologous extremities bilaterally contract. This phenomenon is named bilateral deficit (BLD)[241], and it occurs when the resultant force from bilateral homonymous limb contractions is less than the summed force of individual limb contractions.

According to Kvist[242], the strength contralateral analysis is useful to identify any deficit that could compromise the biomechanics of movement with BLD $\geq$15% considered abnormal. Individuals with KOA have demonstrated strength deficits ranging between 11% and 56% when compared with healthy controls [243], and in cases of pain occurrence, the ability to produce force with the most painful knee is compromised. As expected, results for the strength tests shown in Table 8 were significantly lower in the most painful knee, representing a bilateral deficit for the least painful in all knee strength tests (isokinetic knee extension and flexion and isometric knee extension). However, the worst BLD found was 16% in the isokinetic extension, which, according to Kvist[242], is the only result that can be considered in the limit to the abnormal.

Peak torque values may not adequately reflect tension development through knee range of motion. Total work and mean power generated, on the other hand, are highly relevant measures. Work is done by the rotation-producing force is equal to the torque generated by the force times the angular displacement of the body. The rate at which work is done is known as power. Regarding the total contralateral work, results are in accordance with BLD, being higher in the least painful with differences of 20% in the isokinetic extension strength and of 14% in the isokinetic flexion strength.

It is generally accepted that a strong quadriceps is a protective factor in OA pain[244] and when combined with a strong hamstrings promotes shock absorption and load distribution in the joint, especially during gait[17]. No significant difference in H:Q ratio was found between limbs, although both had an H:Q ratio slightly smaller than the normative value suggested in the literature of 60% to an angular velocity of 60º/s[239, 240].

Despite the fact that only 9 of 48 participants had unilateral KOA, is important to discuss how asymmetry in strength and knee load distributions during walking and in other daily activities can aggravate the disease. For pain avoidance, individuals with unilateral KOA use the strategy of overloading the contralateral limb. Consequently, this overuse of the contralateral knee can cause knee pain and KOA installation in the non-affected knee, leading to bilateral KOA. In the same way, in cases of bilateral KOA, a common strategy is the avoidance of movement in the most painful knee, overloading the Least Painful Knee and increasing pain and aggravating disease in this limb. Curiously, the body composition and morphology outcomes expressed in table 8 indicate that, although there was no difference in fat mass between the MPK and LPK, the circumferences were significantly bigger in the LPK, which allows the speculation that this result could be due to greater muscle mass in the Least Painful Knee, the more overloaded limb.

Reduction or elimination of bilateral deficit could be considered a neural adaptation to strength training, indicating added ability to activate agonists in bilateral movements. Although bilateral activities reduce deficit, performance in unilateral exercises may constitute an important strategy aimed to preserve strength, especially in relevant asymmetry situations [245].

6.2 Effectiveness of PICO Aquatic exercise program

The main discussion of this document is around the effectiveness of the PICO aquatic exercise program on KOA symptoms, quality of life and physical fitness of the obese and overweight adults who participated in this project. Secondary outcomes, body composition, lower limb morphology and lifestyle were discussed in an integrated way, throughout the text, whenever necessary.

Results show that the aquatic exercise protocol conception and implementation by the PICO project provides good indicators for the establishment of guidelines for the design of aquatic exercise programs for obese individuals with KOA. Our findings corroborates the observations of the Lim study [186], showing that aquatic exercise is an effective tool for obese patients who have difficulties with land exercise due to KOA.

A comparison of the aquatic PICO program with other clinical trials that use AE[101] reveals that differences are due to the quality of the aquatic exercise methodology used. The main strengths in the design of this program were the detailed exercise prescription protocol concerning dosage (frequency, duration and intensity of the exercise), the fulfillment of overload and individualized principles of training (e.g., gradual increase in the number of sets and repetitions on strength training), the control of exercise intensity during the sessions by using heart rate monitor equipment and rating perception effort scales (e.g., Borg RPE and OMNI scales), and the pain control by NRS. Another feature of AE is that because the exercise intensity depends on the water´s resistance, which is generated according to the individual’s capacity to apply force against the water (Newton's laws), AE allows for an individualized workout within a group class. On the other hand, control of exercise intensity in the water can be subjective, mainly in strength training, and this has been considered one disadvantage for protocol application.

All evidence-based information provided from previous aquatic studies[121, 148, 151, 183, 186, 190], such as the importance of music on motivation, music cadence effect and the cardiorespiratory responses of each AE pattern, as well its biomechanical characteristics, were considered in the present study. The exercise program was delivered by highly qualified aquatic exercise instructors with controlled supervision to guarantee that interventions were similar in both AE classes, according to the predefined plan.

Strategies implemented in our AE program, namely, the motivational component and the extra class offered every 15 days, to ensure that all participants fulfilled the 24 sessions, are a strength of this program. Additionally, it should be noted that easy access to the program facilities further contributed to participant motivation and adherence. The withdrawal reasons for the four participants who did not complete the whole program were not related to motivation or methodology used, but rather to health problems or an inability to perform the battery of tests at the end of the intervention. One possible constraint to the success of this aquatic exercise program was the level of water skills of each participant. The first month was spent improving the participants' ability to control their body and their ability to apply force against water and reach the desired overload. As a consequence, when participants were ready to work with higher overload, using additional drag equipment, the program was near its end. Increasing the duration of the program by another month would allow time to solve constraints posed by the beginners' water skills.

6.2.1. KOA symptoms and quality of life

The positive changes on KOA symptoms and quality of life outcomes (assessed by KOOS, BPI and BDI questionnaires) found in the present study reflect the multicomponent approach of PICO aquatic exercise program and corroborate the findings of Hinman and coworkers[165] and Kim and coworkers[183].

Beyond being statistically significant, improvements in KOA assessed by KOOS in the AE group were above 10 points in each dimension (Pain=24.3, O.Symptoms=20.1, ADL=23.4, Sport/rec=26.2 and QOL= 14.5) and were considered clinically relevant [202]. In general, changes in KOOS in the AEG were above 40% and quite superior to the changes of symptoms reported in other studies [104, 121, 148, 183, 190]. Although Lund[121] did not observe changes after 16 AE sessions, improvements of 13% after 36 sessions were reported by Wang[104]. The study of Thorstensson[190] showed a significant improvement in QOL after only 12 sessions of land exercise, but the authors did not consider this clinically significance (Table 3). In the study of

Suomi[148], which used a different instrument for pain and ADL assessment, pain improvements in older adults was only approximately 13% after 8 weeks of aquatic exercise.

A detailed analysis of the group effect for each item of KOOS symptoms and KOOS pain (Table 9) provided interesting information about the dose-response to exercise and how it affected the total score of KOOS dimensions. Three items of symptoms showed no group effect (S5, S6 and S7). Concerning the ability to bend the knee (S5), the absence of changes could be due to the fact that our sample population was obese, and their anthropometric measures, weight and fear of falling could have been a constraint to bending the knee. Our expectation is that this should change with long term interventions and subsequent weight loss. In contrast to the aquatic program of Hinnan and coworkers[165], our results for both stiffness items (S6 and S7) did not show significant changes. Those authors attributed their reduction of joint stiffness to the warm water (34ºC), which was higher than the temperature used in our PICO aquatic program (~30.5ºC). With respect to the other symptoms, significant group effects were found for swelling (S1), noise (S2), knee hang up (S3) and knee straightening (S4). The change in these symptoms could be attributed to a decrease in pain, better joint lubrication and improvement in functional strength. The reduction of swelling, may be attributed to the fact that the exercise protocol had been performed in water; if the exercise was performed on land, the joint overload of weight bearing exercises could have caused a contrary effect. Moreover, as described by the principles of hydrodynamics, hydrostatic pressure makes aquatic exercise very different from land-based exercise, and this is important to consider clinically. Hydrostatic pressure increases 1 mmHg every 1.36 cm of water depth. This means that at 1.2 m of body immersion the pressure around the limb is higher than normal diastolic pressure and could aid venous return [246]. This supports the clinical observation that edema or swelling are reduced after immersion [168, 247]. Most likely, joints with reduced swelling can accomplish a larger range of motion, thereby improving movements.

The initial pain level reported at baseline by the participants in our study is considered mild (KOOS Pain= 48±16 and BPI_{sev}= 3.6±2). Based on observations of items in the pain dimension of KOOS (Table 9), the significant group effect observed indicates a successful reduction of pain on all daily living movements such as knee twisting, straightening, walking, and up and downstairs. The improvement of pain at night is critical because pain could impair sleeping quality, thereby affecting mental health and compromising the quality of life.

A significant group effect was found for pain reported in the last 24 hours with changes of nearly 35% for CG and 65% for AEG for both BPI dimensions measured (Fig. 5). These results are superior to those reported by Lim and colleagues [186] who observed a reduction of 25% in pain severity and 35% in pain interference. Hydrostatic pressure can improve peripheral circulation[248] and act on nerve endings and, when combined with muscle relaxation due to the buoyancy of water, can explain the pain reduction reported in both questionnaires, KOOS and BPI [193].

The health-related quality of life in this study was analyzed based on three KOOS dimensions (ADL, Sport/rec and QOL) and on mental health assessed by BDI. The outcomes present significant clinical benefits from the PICO aquatic exercise program and reflect improvements in other outcomes, as mentioned above. Additionally, effect sizes expressed in Table 12 indicate a large effect size for ADL, Sport/rec and BDI and a medium effect size for QOL, revealing the superior results of our aquatic exercise program compared to other studies[104, 165].

With regards to mental health, our findings corroborate the results obtained by Kim and coworkers[183], where depression outcomes benefited from AE. While our improvement on BDI was approximately 46% after 24 sessions, the protocol of Kim and coworkers provided an improvement of only 8% after 36 sessions. However, the questionnaire used and sample characteristics at baseline were different between these 2 studies, and it is possible that once individuals lost weight and were no longer obese, their level of depression was lower. Moreover, the PICO AE had a strong cardiorespiratory component where, beyond its positive effect on pain control[15], aerobic exercise is known to improve mental health by reducing anxiety, depression, and negative mood and by improving self-esteem and cognitive function [73, 92]. In addition, pain involves a psychological dimension and is a subjective perception that can affect pain tolerance; as such, it is correlated with mental health. Improvements in mental health lead to better pain tolerance. Group interactions, music and improvement in physical function can improve an individual’s psychological state. For this reason, besides the improvements in the Beck Depression Inventory (BDI) scores in the AEG (46%), we believe that the tips provided to the CG for a better lifestyle and the possibility to meet other individuals with the same problems, provided motivation to them and contributed to the improvement (10%) in their depressive symptoms. In the same way, this improvement in the BDI of CG may explain their better results in the BPI dimensions.

The improvements in all outcomes and health-related quality of life with PICO aquatic exercise practitioners are clear and are reinforced by testimonials, in appendix 11, and the results of the physical fitness tests.

6.2.2. Physical Fitness

Considering the positive benefits of the PICO aquatic exercise program on KOA symptoms and quality of life, discussed above, we expected that these benefits would be reflected in the physical fitness results. In fact the physical fitness results (Table 10 and 11) are in accordance with other studies [104, 186] and demonstrate the efficacy of AE on the cardiorespiratory, strength and flexibility components of the physical fitness tests. The positive results could be due to the fact that exercises and strategies were chosen to meet specific fitness goals as established in the program design.

It is noteworthy that the strong cardiorespiratory component, with intensity control, used both traveling movements (forward, backward and side-to-side) and basic AE aerobic movements (walking, power walking, cross country skiing, jumping jacks, alternating kick and alternating leg curl). With respect to the 6MWT, the improvement of 55 m in the AEG was a significant group effect (Table 10) and showed the largest effect size (.484, Table 12). This improvement corresponded to an increase in gait speed from 1.5 m/s to 1.7 m/s, with the final speed being higher than most referenced values for individuals with KOA (Table 1), although they were aged individuals, and even in comparison with several studies involving elderly healthy subjects[106, 107, 110]. These findings are better than those reported for short duration protocols[88, 165] and are similar to those reported in the Wang study[104] and to those obtained in the 6-month land program of the IDEA RCT study[103].

Considering the inverse relationship found between the BMI and the 6MWT and that walking is a weight bearing activity, we were concerned that changes in body mass could affect the results. For this reason, the ANCOVA analysis for 6MWT included the body mass changes as a covariate. The results did not indicate a significant effect of body mass change, possibly because the magnitude of weight loss in the AEG, although significant, was not enough to produce an effect on the 6MWT. In addition, the correlation analysis (Table 7) showed that the distance walked in the 6MWT was inversely associated with KOA pain, other symptoms and depressive symptoms and was positively associated with lower limb strength (FRSTST). All of these outcomes showed a significant group effect after intervention.

The positive results obtained in the FRSTST, which evaluated lower limb strength in a closed kinetic chain task, and the Handgrip test could be explained by the inclusion of strengthening exercises in the class planning (Appendix 3) and by the characteristics of the aquatic environment. Although AE is considered a low impact type of exercise, where the reduction in weight bearing is correlated with the immersion level, its characteristics are similar to land neuromuscular exercise. The constant action of hydrodynamic resistance generated by movement and the body stability challenge provided by the buoyancy and inertia of the water means that most of the aerobic patterns of AE are multiplanar and multijoint movements, offering both a resistance-strength workout and stability training for the entire area of the submerged body, even during aerobic exercises.

The FRSTST physical test had the second largest group effect size, after the 6MWT, indicating improvement in the lower limb strength, mainly in the capacity to perform the sit to stand task faster. This finding may be explained by the increase in muscle power due to the exercise cadence variations used in the PICO methodology and, again, the required force application against water resistance.

With respect to the handgrip test, although not a specific test for KOA assessment, this test was found to be a reliable indicator of general physical function, as reported by Deforche and colleagues[227]. Handgrip strength results revealed a significant group effect, which was significantly associated with all physical tests and with self-reported outcomes (KOOS Symptoms, ADL, QOL and with BDI and BPI).

Regarding flexibility, although not one of the major goals defined in the PICO AE program, improvements were reported in both groups for lower limb and upper limb flexibility assessed, respectively with the CSR and BS tests. Nevertheless, the percent change in the AEG (CSR_{LPK}=101%; CSR_{MPK}=104% and BST=40%) was better than in the CG (CSR_{LPK}=88%; CSR_{MPK}=84% and BST=13%) and was higher than the change (9%) reported by Suomi[148] after 8 weeks of AE.

A significant group effect was found for all flexibility tests, with the exception of the CSR_{LPK}, where the absence of a group effect could be due to the large standard deviation. The improvements in the CSR_{MPK} could be related to the pain and symptom relief reported by the AEG. In addition, improvements in flexibility in the AEG could be due to the stretching exercises performed in the end of each class and to the buoyancy action, which allowed assisted exercises to be performed with a large range of motion thereby providing dynamic stretching exercises. It should also be noted that the anthropometric characteristics of overweight and obese individuals could compromise the Back Scratch Test and the Sit and Reach test, both being considered a confounding variable.

Concerning knee strength, the fact that no significant group effect was found for isometric and isokinetic knee extension strength could be explained by the large standard deviation of strength results, due to a possible learning effect from Mom1 to Mom2, and by the presence of pain during the test. Moreover, the absence of a group effect could be due to a slight increase in knee strength in the control group due to some lifestyle change. Although a maximal effort was expected in isokinetic tests, the phenomenon of suboptimal effort is well recognized in the literature. Some patients with known musculoskeletal dysfunction can give less than a full effort during testing time, for a variety of reasons, including pain, fear of pain, anxiety, depression, fear of disease aggravation, lack of understanding of the instructions, and lack of understanding of the importance of the test. Because the group effect comparisons were adjusted for pain, it is possible to speculate that a lack of understanding of the importance of the test or lack of understanding of the instructions could have interfered with baseline tests. After integration into the PICO program, these constraints may have been resolved by the time of testing at Mom2.

Although in most studies with KOA, quadriceps weakness receives much more focus than hamstring weakness, the contribution of knee flexors in knee health status is gaining increasing importance[213, 249]. Contrary to the non-significant changes reported by Lim[186], our program reported knee strength improvements that were different from the results reported by Pais[194] after an aquatic exercise intervention with the same duration (3 months). Their aquatic program had better improvements in the knee extension strength, while our PICO aquatic program only had significant improvements in the knee flexion strength. In addition to differences in the statistical method used, their sample included elderly individuals, where loss in quadriceps strength is accentuated and the capacity to perform movements against buoyancy could be reduced in comparison with younger adults. This means that, if the methodology used did not have a special focus on teaching how to apply force against the water in both directions of movement, it is easier to perform movements of knee extension toward the water surface, where water buoyancy acts to support, than to overload the posterior muscles when returning the limb to the bottom. Most likely, this is the main explanation for our participants who had better improvements in the knee strength at flexion, although subjects with KOA also have well-documented hamstring strength deficits[243].

Additionally, quadriceps weakness, which is considered a risk factor in KOA, is due not only to arthrogenic muscle inhibition (AMI) but also to sarcopenia, a common feature in elderly individuals.

Beyond the strength values of the different muscle groups around the knee joint, assessment of muscle dysfunction should also be considered, in particular, the strength balance between agonist and antagonist muscles, expressed by the hamstring/quadriceps ratio (H:Q), which is an indicator of intermuscular coordination. Decreased hamstring strength relative to the quadriceps (H:Q) may predispose both the joint and the weaker muscle group to injury. Although H:Q could not be considered a predictive factor for incident symptomatic KOA[250], imbalances in the present study were analyzed according Aagaard and colleagues[251], who suggested that a H:Q ratio greater than or equal to 0.6[252] is considered normal. Moreover, expected ratios for the normal knee are 60% to 69% at an angular velocity of 60 degrees per second, with a tendency to increase with increasing angular velocity. Our results, summarized in Table 11, indicate that some H:Q imbalance is present at baseline for both groups, ranging from 0.50-0.60, and despite a slight increase with exercise, it was not enough to be statistically significant and no group effect was observed. Although we know that the knee concentric-concentric protocol used in the present study does not reflect natural muscle function, where the quadriceps contracts concentrically while the hamstring contracts eccentrically in a concentric-eccentric mode (functional H:Q ratio), the concentric-eccentric mode, which is considered more accurate for functional assessment[253], is difficult to perform, especially in a non-athletic population, and could be unsafe for individuals with KOA.

Although weight loss was not the aim of this study, our participants in the AEG had a significant decrease in BMI, in agreement with the study of Lim[186], leading to a reflection of how the AE program could have influenced the weight loss. For this reason, changes in lifestyle were analyzed using the physical activity and the eating patterns outcomes.

The significant group effect observed for the changes in the amount of physical activity could be due to regular attendance at aquatic classes by the AEG, corresponding to 360 METS/week. The physical activity increase recorded, however, was approximately 700 METS, indicating that the AEG did, on average, an extra 340 METS/week on their own. The CG, who attended the educational program, could have also made small changes in their lifestyle, however the IPAQ questionnaire only screened for physical activity of 10 min or more in duration. The main goal of the IPAQ selected for this study was to detect considerable changes in the amount of physical activity, which could be a confounding factor. In other words, the IPAQ was used to screen for participants who began another structured exercise program. In addition, the large standard deviations reported in both groups could have compromised the significance of the results. Despite the significant group effect on changes in the total METs of physical activity, our results show that the weight loss in the AE Group was not due to the change in the physical activity (p=.534).

Another relevant aspect is that the CG received educational and motivational support to change their lifestyle, however this was not offered as an intervention for KOA management. As a result, a significant group effect was found in pain and other symptoms as assessed by KOOS and BPI questionnaires. Consequently, the presence of knee pain and other symptoms remained a constraint for increased physical activity in the CG. On the other hand, although not statistically significance, the CG revealed some improvement in eating patterns, however, this was not enough to compensate for the deficit in physical activity or to be effective in changing BMI. Most likely the energy expended to perform the aquatic exercise patterns, which involve large muscle groups, the possible increase in muscle mass and the small alterations in daily physical activity were enough to improve their BMI. Although no group effect were observed in the sitting time per week, it is important to note that the reduction of sitting time per week in the AEG was 18% while in the CG it was only 1.3%. This difference could be a result of pain reduction and changes in how KOA symptoms affected daily living in the AEG, as reported by KOOS and BPI questionnaires.

6.3 Complementary analyses

6.3.1. BMI groups comparisons for KOA outcomes, physical fitness and quality of life

The difficulty in finding other studies that applied a broad battery of tests with similar sample population, as well the difficulty in finding results presented by BMI groups and similar age intervals, compromised the development of this discussion, however this shows the pertinence of an approach based on BMI group classification.

KOOS outcomes for each BMI group are summarized in table 13. Of all the grade III reported worst conditions in all KOA-related outcomes, only the Pain dimension presented a clear behavior, increasing as BMI increased. A similar tendency was observed for BPI severity (Table 14). These results are consistent with the literature reviewed in Chapter 2, where mechanical pain is related to weight bearing activities[42], being exacerbated by increasing joint load as well systemic inflammation in fat tissues, which may compromise an individual's pain threshold[25, 38, 78].

Higher scores of depressive symptoms were found for obesity grades II and III when compared with grade I and overweight, in accordance with both the results reported by Wadden and coworkers (2006)[74] and the positive and significant correlations between fat mass and BDI, as shown in table 7.

Concerning IPAQ results (Table 14), the groups with higher grade of obesity reported a lower amount of physical activity per week, as expected, and only the overweight group showed a significantly higher level of physical activity per week when compared with all obesity groups ($p<.05$).

In general, the results of the physical tests were better for the overweight group and poorest for obesity grade III. Multiple comparisons of the physical fitness results were performed between groups and are summarized in table 15. Significant differences were found for the 6MWT in the obesity grade III group when compared with the overweight group (p=.011) and with grade I (p=.020) and grade II (p=.033) obesity groups. This fact can be explained by the significant correlations that were found between the 6MWT and Fat Mass and Pain and Depression, and by the absence of a correlation between Fat Mass and the strength and flexibility tests, as summarized in Table 16. In addition, it is possible to say that the distance walked by the obesity grade III group was clinically worse than the distance walked by the other BMI groups (difference>50 m), in agreement with the findings of Messier and coworkers (2013)[103] and somewhat higher than that found in two other studies (20 m)[84, 87], although the last study did not involve KOA. In addition, the obesity grade III group, despite being younger, had worse results than all other studies with reportedly healthy elderly individuals, as cited in table 1.

Regarding isokinetic strength for knee extensors, when comparing results from other studies[114, 118-120], it was interesting to note that our data were lower than all others except for the comparison with the results obtained by White and coworkers[120] for obesity groups grades I-III, which although similar with respect to BMI included an older population, and by Sanchez and coworkers (2003)[113], which had a lower BMI and somewhat older population. In the case of isometric knee extension, the overweight group had better results than that reported in other studies in Table 2 [114, [118, 119], while the obesity groups grade I-II had similar results to those reported by Lim and coworkers[119], but, once again, their sample was older and had a lower mean BMI.

6.3.2. Predictive factors of 6MWT in overweight and obese adults with KOA

The analysis of the three models presented (Table 17) provides important information regarding the walking capacity of obese individuals with KOA. In addition to the walking distance of obese individuals being significantly smaller compared to lean individuals[85, 102], there is an association with the functional limitations imposed by KOA symptoms, leading to the adoption of different gait patterns to ensure maintenance of balance and to avoid mechanical pain, thereby compromising gait efficacy[85] and decreasing gait speed.

Capodaglio and coworkers[102] showed that the 6MWT in obese individuals was significantly correlated with age, gender and BMI, and proposed a reference equation where these variables could explain 48% of the walked distance: 6MWTm= 894.2177 – [2.0700 x age (yrs)] - (51.4489 x gender) - 5.1663 x BMI (Kg/m^2). Our results, summarized in table 16, are in accordance with this study and show a significant correlation between 6MWT and body composition, body morphology and OA symptoms. However, the model of Capodaglio[102] included age as a predictive factor for 6MWT and in our models, age was not significant, possibly due the fact that our regression models were obtained from adults and did not include older persons. This suggests that the effects of aging lost importance and other variables were considered more important for the models. The advantage of using data from the present study to evaluate the predictive factors for 6MWT was the ability to test models with a broad variety of dimensions, from physical fitness and mental health to KOA symptoms and health-related quality of life.

Regarding knee strength, deficits in quadriceps activation can moderate the relationship between knee strength and physical function[254], and this is considered in the literature as a significant predictor for the 6MWT performance[249]. Curiously, despite the correlations that were found for strength tests and 6MWT, the FRSTST remained significant and, instead of the knee strength tests, was included in *Models 1* and *2*. Our participants did not reveal considerable knee muscle weakness, and this could explain the observation that knee strength outcomes did not show relevant results in the 3 models presented. In addition, we did not perform eccentric strength tests, an important component for physical function activities.

Although the variables selected for testing are becoming increasingly simple and accessible, the knee pain obtained from BPI severity is a relevant factor for the 6MWT in each of the 3 models. It was expected that the fat mass included in Model 1 would be substituted with the BMI when the variables from DXA scanner became unavailable for Model 2 and 3, but this was not observed, and Models 2 and 3 did not reveal BMI or other body morphology as predictive factors for 6MWT.

The main conclusion from these analyses is that, in obesity cases, KOA pain should be identified, assessed and controlled in any type of exercise program that involves lower limb movement.

Chapter 7: Conclusions

This chapters presents the research findings which could be concluded according to the results.

7.1 Main research findings

Our study was based on the premise that individuals with KOA need a broad exercise intervention, adapted not only to the affected joint but to overall health status and that works with the whole body and mind, simultaneously. The results of this study provide pertinent information about the viability of establishing a multicomponent approach using aquatic exercise and generating positive results in different components of the human being in addition to OA symptoms. In addition, the sample characteristics of the PICO project as well as overweight and obese adults with KOA represent a real world health problem.

The PICO aquatic exercise program was designed and implemented well, based on the initial project. Our study highlights the importance of developing a controlled and detailed aquatic exercise protocol that, beyond pathology expertise, requires a deep knowledge about the fundamentals of aquatic exercise with aquatic instructors having advanced teaching skills. Control of the training intensity is essential for fitness improvement, and the PICO project demonstrated that the utilization of self-perception subjective effort scales (OMNI and BORG) is possible and effective, even in aquatic exercise group class.

If we consider that an obese person with KOA can have a wide range of associated problems or dysfunctions, an advantage of the PICO project was the complete battery of tests, assessing not only KOA symptoms and related-quality of life but the physical and mental component.

It can be concluded that the participants of the AE program greatly benefited from the PICO protocol, showing improvements in all parameters of KOA symptoms. Our results demonstrate that the strong cardiorespiratory component associated with the specific water properties, namely buoyancy and hydrostatic pressure, contributed to the great improvements in KOA symptoms, including a reduction in pain, knee noise and swelling. Water buoyancy can diminish joint loading of lower extremities thereby reducing the effects of gravity. This is particularly important in exercise management for overweight and obese people because it can reduce the stress placed on joints and decrease the risk for OA progression.

It should be noted that the symptom of knee stiffness did not benefit from our aquatic program. The pool water temperature, approximately 30.5ºC, was adequate for cardiorespiratory training, and although lower than the temperature used in hydrotherapy (≥32ºC), it seemed sufficient for providing pain reduction without compromising exercise intensity.

A result of the relief of symptoms is an improved capacity to perform daily activities, as well as mental health, contributing to a better health-related quality of life. Additionally, we suggest that the motivational strategies used were essential for exercise adherence and the positive results in mental health. The improvements in mental health could be attributed to several others factors: (1) the educational component of the aquatic session; (2) the use of motivational cueing during classes; (3) the variation of the final part in each session and (4) the promotion of social interaction among participants.

This investigation of the effectiveness of the PICO aquatic program on physical fitness produced important results. Aquatic exercise provided improvements in gait, aerobic fitness, general strength (knee strength, handgrip strength and the sit to stand capacity) and flexibility.

With respect to knee strength, positive results were observed for the knee flexors in both the most and least painful knee. Although flexibility improved, there was no specific flexibility training program. This component was incorporated by the use of dynamic stretching during aerobic exercises (assisted by buoyancy), and by stretching exercises added at the end of each session.

The analysis of the predictive factors for the 6MWT concluded that knee pain is a considerable constraint for an obese individual when beginning any type of weight bearing exercise and should be controlled.

The contralateral analysis showed that pain can affect knee strength and lower limb morphology in obese individuals with KOA, confirming that an imbalance in the most painful knee should be an important consideration when designing exercise programs to prevent KOA and worsening physical function.

The PICO Aquatic exercise program was effective for controlling the main obstacles in KOA management (knee pain and depression), being effective on KOA symptoms, and improving health-related quality of life and physical fitness of overweight and obese individuals with KOA.

7.2 Practical implications and future directions

In this section we summarize the practical findings derived from the present dissertation and consider their practical application to the real-world of sports and exercise settings.

The PICO aquatic project provided relevant insights into the exercise intervention field. It showed that aquatic exercise, when well designed using a controlled methodology, is effective at improving all fitness components in adults, not just the elderly. Furthermore, the present study showed that aquatic exercise is a suitable option for obese individuals to control KOA symptoms and initiate a weight loss process. In this way an important message for all weight control programs and for exercise's professionals is that KOA symptoms, mainly pain, must be identified and controlled, otherwise it becomes a constraint for meeting exercise goals.

Pain and depression are considered major obstacles for KOA management, and the PICO aquatic program was effective at solving this constraint. It is our belief that the motivational strategies used and the strong cardiorespiratory component were critical to the results observed.

Unlike other studies, it was shown that it is possible to introduce an educational component during the exercise class period and that it is not necessary to create an extra class just for this goal.

Suggestions for future studies:

- Include gait analyses in the tests battery (kinetics and kinematics);
- Include analyses of biological markers;
- Include strength assessment of hip adductors and abductors, and isokinetic eccentric tests;
- Include assessment of range of motion;

- Include more specific strength training for lower limbs and design the overload progress with drag equipment in the lower limb;
- The exercise program quality depends of the instructor profile, and considering the subjectivity of aquatic exercise stimulus, we advise that instructor selection be carefully conducted;
- Apply this PICO protocol twice a week and include one more month (4 months), corresponding to 32 sessions with a follow-up;
- To reproduce this study with a larger sample, in different community centers, providing reliability for the public health domain; and
- To design and develop the AE protocol for the next step of intervention, after initial KOA symptom management, aimed at body composition improvements.

References

This chapter presents all articles or books which were considered relevant to support this dissertation

1. WHO SGoRD: **Rheumatic diseases : report of a World Health Organizatio (WHO) scientific group.** In *WHO technical report series* pp. 59. Geneva; 1992:59.
2. DGS: **Programa nacional contra as doenças reumáticas:Circular Normativa** (Saúde DGd ed., vol. 12 DGCG edition. Portugal: DGS; 2004.
3. WHO SGoRD: **The burden of musculoskeletal condicion at start of new millenium.** (Series WTR ed. Geneva; 2003.
4. Lucas R, Monjardino MT: *O estado da reumatologia em Portugal.* Porto: Instituto de Saúde Pública da Universidade do Porto; 2010.
5. **The burden of musculoskeletal conditions at the start of the new millennium.** *World Health Organ Tech Rep Ser* 2003, **919:**i-x, 1-218, back cover
6. ONDOR: *Doenças remáticas em Portugal: da investigação às políticas de saúde.* Porto: Instituto de Saúde Pública da Universidade do Porto; 2014.
7. Williams F, Spector T: **Osteoarthritis.** *Medicine* 2006, **34:**364-368.9
8. Costa L, Gal D, Barros H: **Prevalence of rheumatic diseases in an urban population.** *Acta Reum Port29:169-174* 2004**:**169-174.29
9. Sardinha LB, Santos DA, Silva AM, Coelho-e-Silva MJ, Raimundo AM, Moreira H, Santos R, Vale S, Baptista F, Mota J: **Prevalence of overweight, obesity, and abdominal obesity in a representative sample of Portuguese adults.** *PLoS One* 2012, **7:**e47883.10
10. do Carmo I, Dos Santos O, Camolas J, Vieira J, Carreira M, Medina L, Reis L, Myatt J, Galvao-Teles A: **Overweight and obesity in Portugal: national prevalence in 2003-2005.** *Obes Rev* 2008, **9:**11-19.1
11. Instituto Nacional de Estatística (INE): **Censos - Resultados definitivos : Portugal - 2011** vol. . Lisbon: INE - Statistics Portugal; 2012.
12. Zhang W, Nuki G, Moskowitz RW, Abramson S, Altman RD, Arden NK, Bierma-Zeinstra S, Brandt KD, Croft P, Doherty M, et al: **OARSI recommendations for the management of hip and knee osteoarthritis: part III: Changes in evidence following systematic cumulative update of research published through January 2009.** *Osteoarthritis Cartilage* 2010, **18:**476-499.4
13. Zhang W, Moskowitz RW, Nuki G, Abramson S, Altman RD, Arden N, Bierma-Zeinstra S, Brandt KD, Croft P, Doherty M, et al: **OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines.** *Osteoarthritis Cartilage* 2008, **16:**137-162.2
14. Zhang W, Moskowitz RW, Nuki G, Abramson S, Altman RD, Arden N, Bierma-Zeinstra S, Brandt KD, Croft P, Doherty M, et al: **OARSI recommendations for the management of hip and knee osteoarthritis, part I: critical appraisal of existing treatment guidelines and systematic review of current research evidence.** *Osteoarthritis Cartilage* 2007, **15:**981-1000.9
15. Hochberg MC, Altman RD, April KT, Benkhalti M, Guyatt G, McGowan J, Towheed T, Welch V, Wells G, Tugwell P: **American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis**

of the hand, hip, and knee. *Arthritis Care Res (Hoboken)* 2012, **64:**465-474.4

16. Jordan KM, Arden NK, Doherty M, Bannwarth B, Bijlsma JW, Dieppe P, Gunther K, Hauselmann H, Herrero-Beaumont G, Kaklamanis P, et al: **EULAR Recommendations 2003: an evidence based approach to the management of knee osteoarthritis: Report of a Task Force of the Standing Committee for International Clinical Studies Including Therapeutic Trials (ESCISIT).** *Ann Rheum Dis* 2003, **62:**1145-1155.12
17. Arden N, Nevitt MC: **Osteoarthritis: epidemiology.** *Best Pract Res Clin Rheumatol* 2006, **20:**3-25.1
18. Gabriel SE, Michaud K: **Epidemiological studies in incidence, prevalence, mortality, and comorbidity of the rheumatic diseases.** *Arthritis Res Ther* 2009, **11:**229.3
19. Issa SN, Sharma L: **Epidemiology of osteoarthritis: an update.** *Curr Rheumatol Rep* 2006, **8:**7-15.1
20. Wieland HA, Michaelis M, Kirschbaum BJ, Rudolphi KA: **Osteoarthritis - an untreatable disease?** *Nat Rev Drug Discov* 2005, **4:**331-344.4
21. Altman RD, Block DA, Brandt KD, Cooke DV, Greenwald RA, Hochberg MC, Howell DS, Ike RW, Kaplan D, Koopman W, et al.: **Osteoarthritis: definitions and criteria.** *Ann Rheum Dis* 1990, **49:**201.3
22. Reginster JY, Bruyere O, Henrotin Y: **New perspectives in the management of osteoarthritis. structure modification: facts or fantasy?** *J Rheumatol Suppl* 2003, **67:**14-20
23. Dieppe P: **Osteoarthritis.** *Acta Orthop Scand Suppl* 1998, **281:**2-5
24. Karsdal MA, Leeming DJ, Dam EB, Henriksen K, Alexandersen P, Pastoureau P, Altman RD, Christiansen C: **Should subchondral bone turnover be targeted when treating osteoarthritis?** *Osteoarthritis Cartilage* 2008, **16:**638-646.6
25. van der Kraan PM: **Osteoarthritis year 2012 in review: biology.** *Osteoarthritis Cartilage* 2012, **20:**1447-1450.12
26. Rai MF, Sandell LJ: **Inflammatory mediators: tracing links between obesity and osteoarthritis.** *Crit Rev Eukaryot Gene Expr* 2011, **21:**131-142.2
27. Zhang Y, Jordan JM: **Epidemiology of osteoarthritis.** *Clin Geriatr Med* 2010, **26:**355-369.3
28. Jordan JM, Helmick CG, Renner JB, Luta G, Dragomir AD, Woodard J, Fang F, Schwartz TA, Abbate LM, Callahan LF, et al: **Prevalence of knee symptoms and radiographic and symptomatic knee osteoarthritis in African Americans and Caucasians: the Johnston County Osteoarthritis Project.** *J Rheumatol* 2007, **34:**172-180.1
29. Bitton R: **The economic burden of osteoarthritis.** *Am J Manag Care* 2009, **15:**S230-235.8 Suppl
30. Andriacchi TP: **Dynamics of knee malalignment.** *Orthop Clin North Am* 1994, **25:**395-403.3

31. Winby CR, Lloyd DG, Besier TF, Kirk TB: **Muscle and external load contribution to knee joint contact loads during normal gait.** *J Biomech* 2009, **42:**2294-2300.14

32. Martin KR, Kuh D, Harris TB, Guralnik JM, Coggon D, Wills AK: **Body mass index, occupational activity, and leisure-time physical activity: an exploration of risk factors and modifiers for knee osteoarthritis in the 1946 British birth cohort.** *BMC Musculoskelet Disord* 2013, **14:**219

33. Cooper C, Snow S, McAlindon TE, Kellingray S, Stuart B, Coggon D, Dieppe PA: **Risk factors for the incidence and progression of radiographic knee osteoarthritis.** *Arthritis Rheum* 2000, **43:**995-1000.5

34. Muthuri SG, Hui M, Doherty M, Zhang W: **What if we prevent obesity? Risk reduction in knee osteoarthritis estimated through a meta-analysis of observational studies.** *Arthritis Care Res (Hoboken)* 2011, **63:**982-990.7

35. Sturmer T, Gunther KP, Brenner H: **Obesity, overweight and patterns of osteoarthritis: the Ulm Osteoarthritis Study.** *J Clin Epidemiol* 2000, **53:**307-313.3

36. Zhang W, McWilliams DF, Ingham SL, Doherty SA, Muthuri S, Muir KR, Doherty M: **Nottingham knee osteoarthritis risk prediction models.** *Ann Rheum Dis* 2011, **70:**1599-1604.9

37. Englund M: **The role of biomechanics in the initiation and progression of OA of the knee.** *Best Pract Res Clin Rheumatol* 2010, **24:**39-46.1

38. Messier SP: **Obesity and osteoarthritis: disease genesis and nonpharmacologic weight management.** *Rheum Dis Clin North Am* 2008, **34:**713-729.3

39. Tanamas S, Hanna FS, Cicuttini FM, Wluka AE, Berry P, Urquhart DM: **Does knee malalignment increase the risk of development and progression of knee osteoarthritis? A systematic review.** *Arthritis Rheum* 2009, **61:**459-467.4

40. Moskowitz R, Altman R, Buckwalter J, Goldberg V, Hochberg M: *Osteoarthritis: Diagnosis and Medical/surgical Management.* 4 edn. Philadelphia, USA: Lippincott Williams & Wilkins; 2007.

41. Castro RR, Cunha FQ, Silva FS, Jr., Rocha FA: **A quantitative approach to measure joint pain in experimental osteoarthritis--evidence of a role for nitric oxide.** *Osteoarthritis Cartilage* 2006, **14:**769-776.8

42. Chan KK, Chan LW: **A qualitative study on patients with knee osteoarthritis to evaluate the influence of different pain patterns on patients' quality of life and to find out patients' interpretation and coping strategies for the disease.** *Rheumatology Reports* 2011, **3**.1

43. Hurley MV, Newham DJ: **The influence of arthrogenous muscle inhibition on quadriceps rehabilitation of patients with early, unilateral osteoarthritic knees.** *Br J Rheumatol* 1993, **32:**127-131.2

44. Manetta J, Franz LH, Moon C, Perell KL, Fang M: **Comparison of hip and knee muscle moments in subjects with and without knee pain.** *Gait Posture* 2002, **16:**249-254.3

45. McNair PJ, Marshall RN, Maguire K: **Swelling of the knee joint: effects of exercise on quadriceps muscle strength.** *Arch Phys Med Rehabil* 1996, **77:**896-899.9

46. Petty NJ: *Principles of Neuromusculoskeletal Treatment and Management: A Handbook for Therapists.* Elsevier Health Sciences UK; 2011.

47. **WHOQOL: Measuring quality of life** [http://www.who.int/mental_health/media/68.pdf]^1997Access

48. Cella DF: **Quality of life: Concepts and definition.** *Journal of Pain and Symptom Management* 1994, **9:**186-192.3

49. Altman RD: **Criteria for the classification of osteoarthritis of the knee and hip.** *Scand J Rheumatol Suppl* 1987, **65:**31-39

50. Bauer DC, Hunter DJ, Abramson SB, Attur M, Corr M, Felson D, Heinegard D, Jordan JM, Kepler TB, Lane NE, et al: **Classification of osteoarthritis biomarkers: a proposed approach.** *Osteoarthritis Cartilage* 2006, **14:**723-727.8

51. Ai F, Yu C, Zhang W, Morelli JN, Kacher D, Li X: **MR imaging of knee osteoarthritis and correlation of findings with reported patient pain.** *J Huazhong Univ Sci Technolog Med Sci*, **30:**248-254.2

52. Zhang W, Doherty M, Peat G, Bierma-Zeinstra MA, Arden NK, Bresnihan B, Herrero-Beaumont G, Kirschner S, Leeb BF, Lohmander LS, et al: **EULAR evidence-based recommendations for the diagnosis of knee osteoarthritis.** *Ann Rheum Dis* 2010, **69:**483-489.3

53. Schiphof D, van Middelkoop M, de Klerk BM, Oei EH, Hofman A, Koes BW, Weinans H, Bierma-Zeinstra SM: **Crepitus Is a First Indication of Patellofemoral Osteoarthritis (and Not of Tibiofemoral Osteoarthritis).** *Osteoarthritis Cartilage* 2014

54. Rajabi R, Johnson GM, Alizadeh MH, Meghdadi N: **Radiographic knee osteoarthritis in ex-elite table tennis players.** *BMC Musculoskelet Disord* 2012, **13:**12

55. Horvath G, Koroknai G, Acs B, Than P, Bellyei A, Illes T: **Prevalence of radiographic primary hip and knee osteoarthritis in a representative Central European population.** *Int Orthop* 2011, **35:**971-975.7

56. Cibere J, Zhang H, Thorne A, Wong H, Singer J, Kopec JA, Guermazi A, Peterfy C, Nicolaou S, Munk PL, Esdaile JM: **Association of clinical findings with pre-radiographic and radiographic knee osteoarthritis in a population-based study.** *Arthritis Care Res (Hoboken)*, **62:**1691-1698.12

57. Hunter DJ, Arden N, Conaghan PG, Eckstein F, Gold G, Grainger A, Guermazi A, Harvey W, Jones G, Hellio Le Graverand MP, et al: **Definition of osteoarthritis on MRI: results of a Delphi exercise.** *Osteoarthritis Cartilage* 2011, **19:**963-969.8

58. Schiphof D, Oei EH, Hofman A, Waarsing JH, Weinans H, Bierma-Zeinstra SM: **Sensitivity and associations with pain and body weight of an MRI definition of knee osteoarthritis compared with radiographic**

Kellgren and Lawrence criteria: a population-based study in middle-aged females. *Osteoarthritis Cartilage* 2014, **22:**440-446.3

59. Javaid MK, Lynch JA, Tolstykh I, Guermazi A, Roemer F, Aliabadi P, McCulloch C, Curtis J, Felson D, Lane NE, et al: **Pre-radiographic MRI findings are associated with onset of knee symptoms: the most study.** *Osteoarthritis Cartilage*, **18:**323-328.3

60. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW: **Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee.** *J Rheumatol* 1988, **15:**1833-1840.12

61. Goncalves RS, Cabri J, Pinheiro JP, Ferreira PL, Gil J: **Reliability, validity and responsiveness of the Portuguese version of the Knee injury and Osteoarthritis Outcome Score--Physical Function Short-form (KOOS-PS).** *Osteoarthritis Cartilage*, **18:**372-376.3

62. Roos EM, Roos HP, Lohmander LS, Ekdahl C, Beynnon BD: **Knee Injury and Osteoarthritis Outcome Score (KOOS)--development of a self-administered outcome measure.** *J Orthop Sports Phys Ther* 1998, **28:**88-96.2

63. Rat AC, Coste J, Pouchot J, Baumann M, Spitz E, Retel-Rude N, Le Quintrec JS, Dumont-Fischer D, Guillemin F: **OAKHQOL: a new instrument to measure quality of life in knee and hip osteoarthritis.** *J Clin Epidemiol* 2005, **58:**47-55.1

64. Bellamy N, Bell MJ, Pericak D, Goldsmith CH, Torrance GW, Raynauld JP, Walker V, Tugwell P, Polisson R: **BLISS index for analyzing knee osteoarthritis trials data.** *J Clin Epidemiol* 2007, **60:**124-132.2

65. Greco NJ, Anderson AF, Mann BJ, Cole BJ, Farr J, Nissen CW, Irrgang JJ: **Responsiveness of the International Knee Documentation Committee Subjective Knee Form in comparison to the Western Ontario and McMaster Universities Osteoarthritis Index, modified Cincinnati Knee Rating System, and Short Form 36 in patients with focal articular cartilage defects.** *Am J Sports Med*, **38:**891-902.5

66. Roos EM, Toksvig-Larsen S: **Knee injury and Osteoarthritis Outcome Score (KOOS) - validation and comparison to the WOMAC in total knee replacement.** *Health Qual Life Outcomes* 2003, **1:**17

67. Theiler R, Spielberger J, Bischoff HA, Bellamy N, Huber J, Kroesen S: **Clinical evaluation of the WOMAC 3.0 OA Index in numeric rating scale format using a computerized touch screen version.** *Osteoarthritis Cartilage* 2002, **10:**479-481.6

68. **The Global Epidemic: IASO/IOTF analysis** [http://www.iaso.org/iotf/obesity/obesitytheglobalepidemic/]^2010Access

69. Pereira D, Severo M, Barros H, Branco J, Santos R, Ramos E: **The effect of depressive symptoms on the association between radiographic osteoarthritis and knee pain: a cross-sectional study.** *BMC Musculoskelet Disord* 2013, **14:**214.1

70. Farr JN, Going SB, Lohman TG, Rankin L, Kasle S, Cornett M, Cussler E: **Physical activity levels in patients with early knee osteoarthritis measured by accelerometry.** *Arthritis Rheum* 2008, **59:**1229-1236.9

71. Flegal KM, Carroll MD, Ogden CL, Johnson CL: **Prevalence and trends in obesity among US adults, 1999-2000.** *JAMA* 2002, **288:**1723-1727.14

72. Pisters MF, Veenhof C, van Dijk GM, Dekker J: **Avoidance of activity and limitations in activities in patients with osteoarthritis of the hip or knee: a 5 year follow-up study on the mediating role of reduced muscle strength.** *Osteoarthritis Cartilage* 2014, **22:**171-177.2

73. Scopaz KA, Piva SR, Wisniewski S, Fitzgerald GK: **Relationships of fear, anxiety, and depression with physical function in patients with knee osteoarthritis.** *Arch Phys Med Rehabil* 2009, **90:**1866-1873.11

74. Wadden TA, Foster GD: **Weight and Lifestyle Inventory (WALI).** *Obesity (Silver Spring)* 2006, **14 Suppl 2:**99S-118S

75. Lee S, Kim TN, Kim SH: **Sarcopenic obesity is more closely associated with knee osteoarthritis than is nonsarcopenic obesity: a cross-sectional study.** *Arthritis Rheum* 2012, **64:**3947-3954.12

76. Bullo M, Garcia-Lorda P, Megias I, Salas-Salvado J: **Systemic inflammation, adipose tissue tumor necrosis factor, and leptin expression.** *Obes Res* 2003, **11:**525-531.4

77. Scharstuhl A, Glansbeek HL, van Beuningen HM, Vitters EL, van der Kraan PM, van den Berg WB: **Inhibition of endogenous TGF-beta during experimental osteoarthritis prevents osteophyte formation and impairs cartilage repair.** *J Immunol* 2002, **169:**507-514.1

78. Mobasheri A: **Osteoarthritis year 2012 in review: biomarkers.** *Osteoarthritis Cartilage* 2012, **20:**1451-1464.12

79. Coggon D, Reading I, Croft P, McLaren M, Barrett D, Cooper C: **Knee osteoarthritis and obesity.** *Int J Obes Relat Metab Disord* 2001, **25:**622-627.5

80. Messier SP, Gutekunst DJ, Davis C, DeVita P: **Weight loss reduces knee-joint loads in overweight and obese older adults with knee osteoarthritis.** *Arthritis Rheum* 2005, **52:**2026-2032.7

81. Vartiainen P, Bragge T, Lyytinen T, Hakkarainen M, Karjalainen PA, Arokoski JP: **Kinematic and kinetic changes in obese gait in bariatric surgery-induced weight loss.** *J Biomech* 2012, **45:**1769-1774.10

82. Harding GT, Hubley-Kozey CL, Dunbar MJ, Stanish WD, Astephen Wilson JL: **Body mass index affects knee joint mechanics during gait differently with and without moderate knee osteoarthritis.** *Osteoarthritis Cartilage* 2012, **20:**1234-1242.11

83. Messier SP, Loeser RF, Hoover JL, Semble EL, Wise CM: **Osteoarthritis of the knee: effects on gait, strength, and flexibility.** *Arch Phys Med Rehabil* 1992, **73:**29-36.1

84. Beriault K, Carpentier AC, Gagnon C, Menard J, Baillargeon JP, Ardilouze JL, Langlois MF: **Reproducibility of the 6-minute walk test in obese adults.** *Int J Sports Med* 2009, **30:**725-727.10

85. Hulens M, Vansant G, Claessens AL, Lysens R, Muls E: **Predictors of 6-minute walk test results in lean, obese and morbidly obese women.** *Scand J Med Sci Sports* 2003, **13:**98-105.2

86. Larsson UE, Reynisdottir S: **The six-minute walk test in outpatients with obesity: reproducibility and known group validity.** *Physiother Res Int* 2008, **13:**84-93.2

87. Miller GD, Nicklas BJ, Davis C, Loeser RF, Lenchik L, Messier SP: **Intensive weight loss program improves physical function in older obese adults with knee osteoarthritis.** *Obesity (Silver Spring)* 2006, **14:**1219-1230.7

88. Schlenk EA, Lias JL, Sereika SM, Dunbar-Jacob J, Kwoh CK: **Improving physical activity and function in overweight and obese older adults with osteoarthritis of the knee: a feasibility study.** *Rehabil Nurs* 2011, **36:**32-42.1

89. Axford J, Heron C, Ross F, Victor CR: **Management of knee osteoarthritis in primary care: pain and depression are the major obstacles.** *J Psychosom Res* 2008, **64:**461-467.5

90. Bennell KL, Hinman RS: **A review of the clinical evidence for exercise in osteoarthritis of the hip and knee.** *J Sci Med Sport* 2011, **14:**4-9.1

91. Roddy E, Zhang W, Doherty M: **Aerobic walking or strengthening exercise for osteoarthritis of the knee? A systematic review.** *Ann Rheum Dis* 2005, **64:**544-548.4

92. Creamer P, Lethbridge-Cejku M, Hochberg MC: **Factors associated with functional impairment in symptomatic knee osteoarthritis.** *Rheumatology (Oxford)* 2000, **39:**490-496.5

93. Ratzlaff CR, Liang MH: **New developments in osteoarthritis. Prevention of injury-related knee osteoarthritis: opportunities for the primary and secondary prevention of knee osteoarthritis.** *Arthritis Res Ther* 2010, **12:**215.4

94. Bennell KL, Messier SP: **Osteoarthritis: Strength training, self-management or both for early knee OA.** *Nat Rev Rheumatol* 2010, **6:**313-314.6

95. Wang X, Miller GD, Messier SP, Nicklas BJ: **Knee strength maintained despite loss of lean body mass during weight loss in older obese adults with knee osteoarthritis.** *J Gerontol A Biol Sci Med Sci* 2007, **62:**866-871.8

96. Lim BW, Hinman RS, Wrigley TV, Sharma L, Bennell KL: **Does knee malalignment mediate the effects of quadriceps strengthening on knee adduction moment, pain, and function in medial knee osteoarthritis? A randomized controlled trial.** *Arthritis Rheum* 2008, **59:**943-951.7

97. Block JA, Shakoor N: **The biomechanics of osteoarthritis: implications for therapy.** *Curr Rheumatol Rep* 2009, **11:**15-22.1

98. Reeves ND, Bowling FL: **Conservative biomechanical strategies for knee osteoarthritis.** *Nat Rev Rheumatol* 2011, **7:**113-122.2

99. Cibere J, Bellamy N, Thorne A, Esdaile JM, McGorm KJ, Chalmers A, Huang S, Peloso P, Shojania K, Singer J, et al: **Reliability of the knee examination in osteoarthritis: effect of standardization.** *Arthritis Rheum* 2004, **50:**458-468.2

100. American College of Sports Medicine (ACSM): *ACSM's Guidelines for Exercise Testing and Prescription.* 8th edn: Lippincott Williams & Wilkins; 2009.

101. Escalante Y, Garcia-Hermoso A, Saavedra JM: **Effects of exercise on functional aerobic capacity in lower limb osteoarthritis: a systematic review.** *J Sci Med Sport* 2011, **14:**190-198.3

102. Capodaglio P, De Souza SA, Parisio C, Precilios H, Vismara L, Cimolin V, Brunani A: **Reference values for the 6-Min Walking Test in obese subjects.** *Disabil Rehabil* 2013, **35:**1199-1203.14

103. Messier SP, Mihalko SL, Legault C, Miller GD, Nicklas BJ, DeVita P, Beavers DP, Hunter DJ, Lyles MF, Eckstein F, et al: **Effects of intensive diet and exercise on knee joint loads, inflammation, and clinical outcomes among overweight and obese adults with knee osteoarthritis: the IDEA randomized clinical trial.** *JAMA* 2013, **310:**1263-1273.12

104. Wang TJ, Lee SC, Liang SY, Tung HH, Wu SF, Lin YP: **Comparing the efficacy of aquatic exercises and land-based exercises for patients with knee osteoarthritis.** *J Clin Nurs* 2011, **20:**2609-2622.17-18

105. Kennedy DM, Stratford PW, Wessel J, Gollish JD, Penney D: **Assessing stability and change of four performance measures: a longitudinal study evaluating outcome following total hip and knee arthroplasty.** *BMC Musculoskelet Disord* 2005, **6:**3

106. Kervio G, Carre F, Ville NS: **Reliability and intensity of the six-minute walk test in healthy elderly subjects.** *Med Sci Sports Exerc* 2003, **35:**169-174.1

107. Jones CJ, Rikli RE, Max J, Noffal G: **The reliability and validity of a chair sit-and-reach test as a measure of hamstring flexibility in older adults.** *Res Q Exerc Sport* 1998, **69:**338-343.4

108. Troosters T, Gosselink R, Decramer M: **Six minute walking distance in healthy elderly subjects.** *Eur Respir J* 1999, **14:**270-274.2

109. Camarri B, Eastwood PR, Cecins NM, Thompson PJ, Jenkins S: **Six minute walk distance in healthy subjects aged 55-75 years.** *Respir Med* 2006, **100:**658-665.4

110. Carvalho MJ, Marques E, Mota J: **Training and detraining effects on functional fitness after a multicomponent training in older women.** *Gerontology* 2009, **55:**41-48.1

111. Hurley MV: **The role of muscle weakness in the pathogenesis of osteoarthritis.** *Rheum Dis Clin North Am* 1999, **25:**283-298, vi.2

112. Messier SP, Mihalko SL, Beavers DP, Nicklas BJ, Devita P, Carr JJ, Hunter DJ, Williamson JD, Bennell KL, Guermazi A, et al: **Strength Training for Arthritis Trial (START): design and rationale.** *BMC Musculoskelet Disord* 2013, **14:**208.1

113. Sanchez-Ramirez DC, van der Leeden M, van der Esch M, Gerritsen M, Roorda LD, Verschueren S, van Dieen J, Dekker J, Lems WF: **Association of serum C-reactive protein and erythrocyte sedimentation rate with muscle strength in patients with knee osteoarthritis.** *Rheumatology (Oxford)* 2013, **52:**727-732.4

114. Bennell KL, Kyriakides M, Metcalf B, Egerton T, Wrigley TV, Hodges PW, Hunt MA, Roos EM, Forbes A, Ageberg E, Hinman RS: **Neuromuscular versus quadriceps strengthening exercise in people with medial knee osteoarthritis and varus malalignment: A randomised controlled trial.** *Arthritis Rheum* 2013

115. Diracoglu D, Baskent A, Yagci I, Ozcakar L, Aydin R: **Isokinetic strength measurements in early knee osteoarthritis.** *Acta Reumatol Port* 2009, **34:**72-77.1

116. Malas FU, Ozcakar L, Kaymak B, Ulasli A, Guner S, Kara M, Akinci A: **Effects of different strength training on muscle architecture: clinical and ultrasonographic evaluation in knee osteoarthritis.** *PM R* 2013, **5:**655-662.8

117. Glass NA, Torner JC, Frey Law LA, Wang K, Yang T, Nevitt MC, Felson DT, Lewis CE, Segal NA: **The relationship between quadriceps muscle weakness and worsening of knee pain in the MOST cohort: a 5-year longitudinal study.** *Osteoarthritis Cartilage* 2013, **21:**1154-1159.9

118. Kean CO, Birmingham TB, Garland SJ, Bryant DM, Giffin JR: **Minimal detectable change in quadriceps strength and voluntary muscle activation in patients with knee osteoarthritis.** *Arch Phys Med Rehabil* 2010, **91:**1447-1451.9

119. Lim BW, Kemp G, Metcalf B, Wrigley TV, Bennell KL, Crossley KM, Hinman RS: **The association of quadriceps strength with the knee adduction moment in medial knee osteoarthritis.** *Arthritis Rheum* 2009, **61:**451-458.4

120. White DK, Neogi T, Zhang Y, Felson D, Lavalley M, Niu J, Nevitt M, Lewis CE, Torner J, Douglas Gross K: **The association of obesity with walking independent of knee pain: the multicenter osteoarthritis study.** *J Obes* 2012, **2012:**261974

121. Lund H, Weile U, Christensen R, Rostock B, Downey A, Bartels EM, Danneskiold-Samsoe B, Bliddal H: **A randomized controlled trial of aquatic and land-based exercise in patients with knee osteoarthritis.** *J Rehabil Med* 2008, **40:**137-144.2

122. Trans T, Aaboe J, Henriksen M, Christensen R, Bliddal H, Lund H: **Effect of whole body vibration exercise on muscle strength and proprioception in females with knee osteoarthritis.** *Knee* 2009, **16:**256-261.4

123. Messier SP, Legault C, Schoenlank CR, Newman JJ, Martin DF, DeVita P: **Risk factors and mechanisms of knee injury in runners.** *Med Sci Sports Exerc* 2008, **40:**1873-1879.11

124. Zhang W, Doherty M, Arden N, Bannwarth B, Bijlsma J, Gunther KP, Hauselmann HJ, Herrero-Beaumont G, Jordan K, Kaklamanis P, et al: **EULAR evidence based recommendations for the management of hip osteoarthritis: report of a task force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT).** *Ann Rheum Dis* 2005, **64:**669-681.5

125. Nicholas MK: **Pain management in musculoskeletal conditions.** *Best Pract Res Clin Rheumatol* 2008, **22:**451-470.3

126. Ariyoshi M, Sonoda K, Nagata K, Mashima T, Zenmyo M, Paku C, Takamiya Y, Yoshimatsu H, Hirai Y, Yasunaga H, et al: **Efficacy of**

aquatic exercises for patients with low-back pain. *Kurume Med J* 1999, **46:**91-96.2

127. Bacon MC, Nicholson C, Binder H, White PH: **Juvenile rheumatoid arthritis. Aquatic exercise and lower-extremity function.** *Arthritis Care Res* 1991, **4:**102-105.2

128. Hall J, Grant J, Blake D, Taylor G, Garbutt G: **Cardiorespiratory responses to aquatic treadmill walking in patients with rheumatoid arthritis.** *Physiother Res Int* 2004, **9:**59-73.2

129. Kelly M, Darrah J: **Aquatic exercise for children with cerebral palsy.** *Dev Med Child Neurol* 2005, **47:**838-842.12

130. Cantarero-Villanueva I, Fernandez-Lao C, Cuesta-Vargas AI, Del Moral-Avila R, Fernandez-de-Las-Penas CC, Arroyo-Morales M: **The Effectiveness Of A Deep Water Aquatic Exercise Program In Cancer-Related Fatigue In Breast Cancer Survivors: A Randomized Clinical Trial Deep water aquatic exercise in cancer survivors.** *Arch Phys Med Rehabil* 2012

131. DeMaere JM, Ruby BC: **Effects of deep water and treadmill running on oxygen uptake and energy expenditure in seasonally trained cross country runners.** *J Sports Med Phys Fitness* 1997, **37:**175-181.3

132. Martel GF, Harmer ML, Logan JM, Parker CB: **Aquatic plyometric training increases vertical jump in female volleyball players.** *Med Sci Sports Exerc* 2005, **37:**1814-1819.10

133. Reilly T, Ekblom B: **The use of recovery methods post-exercise.** *J Sports Sci* 2005, **23:**619-627.6

134. Alberton CL, Cadore EL, Pinto SS, Tartaruga MP, da Silva EM, Kruel LF: **Cardiorespiratory, neuromuscular and kinematic responses to stationary running performed in water and on dry land.** *European Journal of Applied Physiology* 2011, **111:**1157-1166.6

135. Yazigi F, Pinto S, Colado J, Escalante Y, Armada-Da-Silva P, Brasil R, Alves F: **The cadence and water temperature effect on physiological responses during water cycling.** *Eur J Sport Sci* 2013**:**1-7

136. Broman G, Quintana M, Engardt M, Gullstrand L, Jansson E, Kaijser L: **Older women's cardiovascular responses to deep-water running.** *J Aging Phys Act* 2006, **14:**29-40.1

137. Brown SP, Chitwood LF, Beason KR, McLemore DR: **Physiological correlates with perceived exertion during deep water running.** *Percept Mot Skills* 1996, **83:**155-162.1

138. Butts NK, Tucker M, Greening C: **Physiologic responses to maximal treadmill and deep water running in men and women.** *Am J Sports Med* 1991, **19:**612-614.6

139. Chu KS, Rhodes EC: **Physiological and cardiovascular changes associated with deep water running in the young. Possible implications for the elderly.** *Sports Med* 2001, **31:**33-46.1

140. Triplett NT, Colado JC, Benavent J, Alakhdar Y, Madera J, Gonzalez LM, Tella V: **Concentric and impact forces of single-leg jumps in an aquatic environment versus on land.** *Med Sci Sports Exerc* 2009, **41:**1790-1796.9

141. Phillips VK, Legge M, Jones LM: **Maximal physiological responses between aquatic and land exercise in overweight women.** *Med Sci Sports Exerc* 2008, **40:**959-964.5

142. Aquatic Exercise Association (AEA): *Aquatic Fitness Professional Manual* 5 edn. Nokomis, FL: AEA; 2006.

143. Burns AS, Lauder TD: **Deep water running: an effective non-weightbearing exercise for the maintenance of land-based running performance.** *Mil Med* 2001, **166:**253-258.3

144. Bushman BA, Flynn MG, Andres FF, Lambert CP, Taylor MS, Braun WA: **Effect of 4 wk of deep water run training on running performance.** *Med Sci Sports Exerc* 1997, **29:**694-699.5

145. Frangolias DD, Taunton JE, Rhodes EC, McConkey JP, Moon M: **Maintenance of aerobic capacity during recovery from right foot Jones fracture: a case report.** *Clin J Sport Med* 1997, **7:**54-57; discussion 57-58.1

146. Wilber RL, Moffatt RJ, Scott BE, Lee DT, Cucuzzo NA: **Influence of water run training on the maintenance of aerobic performance.** *Med Sci Sports Exerc* 1996, **28:**1056-1062.8

147. Bravo G, Gauthier P, Roy PM, Payette H, Gaulin P: **A weight-bearing, water-based exercise program for osteopenic women: its impact on bone, functional fitness, and well-being.** *Arch Phys Med Rehabil* 1997, **78:**1375-1380.12

148. Suomi R, Collier D: **Effects of arthritis exercise programs on functional fitness and perceived activities of daily living measures in older adults with arthritis.** *Arch Phys Med Rehabil* 2003, **84:**1589-1594.11

149. Suomi R, Koceja DM: **Postural sway characteristics in women with lower extremity arthritis before and after an aquatic exercise intervention.** *Arch Phys Med Rehabil* 2000, **81:**780-785.6

150. Gusi N, Tomas-Carus P, Hakkinen A, Hakkinen K, Ortega-Alonso A: **Exercise in waist-high warm water decreases pain and improves health-related quality of life and strength in the lower extremities in women with fibromyalgia.** *Arthritis Rheum* 2006, **55:**66-73.1

151. Wang TJ, Belza B, Elaine Thompson F, Whitney JD, Bennett K: **Effects of aquatic exercise on flexibility, strength and aerobic fitness in adults with osteoarthritis of the hip or knee.** *J Adv Nurs* 2007, **57:**141-152.2

152. Driver S, O'Connor J, Lox C, Rees K: **Evaluation of an aquatics programme on fitness parameters of individuals with a brain injury.** *Brain Inj* 2004, **18:**847-859.9

153. Templeton MS, Booth DL, O'Kelly WD: **Effects of aquatic therapy on joint flexibility and functional ability in subjects with rheumatic disease.** *J Orthop Sports Phys Ther* 1996, **23:**376-381.6

154. Colado JC, Tella V, Triplett NT, Gonzalez LM: **Effects of a short-term aquatic resistance program on strength and body composition in fit young men.** *J Strength Cond Res* 2009, **23:**549-559.2

155. Volaklis KA, Spassis AT, Tokmakidis SP: **Land versus water exercise in patients with coronary artery disease: effects on body**

composition, blood lipids, and physical fitness. *Am Heart J* 2007, **154:**560 e561-566.3

156. Tsourlou T, Benik A, Dipla K, Zafeiridis A, Kellis S: **The effects of a twenty-four-week aquatic training program on muscular strength performance in healthy elderly women.** *J Strength Cond Res* 2006, **20:**811-818.4

157. Devereux K, Robertson D, Briffa NK: **Effects of a water-based program on women 65 years and over: a randomised controlled trial.** *Aust J Physiother* 2005, **51:**102-108.2

158. Noh DK, Lim JY, Shin HI, Paik NJ: **The effect of aquatic therapy on postural balance and muscle strength in stroke survivors--a randomized controlled pilot trial.** *Clin Rehabil* 2008, **22:**966-976.10-11

159. Tomas-Carus P, Hakkinen A, Gusi N, Leal A, Hakkinen K, Ortega-Alonso A: **Aquatic training and detraining on fitness and quality of life in fibromyalgia.** *Med Sci Sports Exerc* 2007, **39:**1044-1050.7

160. Cancela Carral JM, Ayan Perez C: **Effects of high-intensity combined training on women over 65.** *Gerontology* 2007, **53:**340-346.6

161. Lee HY: **[Comparison of effects among Tai-Chi exercise, aquatic exercise, and a self-help program for patients with knee osteoarthritis].** *Taehan Kanho Hakhoe Chi* 2006, **36:**571-580.3

162. Driver S, Rees K, O'Connor J, Lox C: **Aquatics, health-promoting self-care behaviours and adults with brain injuries.** *Brain Inj* 2006, **20:**133-141.2

163. Lim JY, Tchai E, Jang SN: **Effectiveness of Aquatic Exercise for Obese Patients with Knee Osteoarthritis: A Randomized Controlled Trial.** *PM R*, **2:**723-731.8

164. Ay A, Yurtkuran M: **Influence of aquatic and weight-bearing exercises on quantitative ultrasound variables in postmenopausal women.** *Am J Phys Med Rehabil* 2005, **84:**52-61.1

165. Hinman RS, Heywood SE, Day AR: **Aquatic physical therapy for hip and knee osteoarthritis: results of a single-blind randomized controlled trial.** *Phys Ther* 2007, **87:**32-43.1

166. Watanabe E, Takeshima N, Okada A, Inomata K: **Comparison of water- and land-based exercise in the reduction of state anxiety among older adults.** *Percept Mot Skills* 2000, **91:**97-104.1

167. Barbosa TM, Garrido MF, Bragada J: **Physiological adaptations to head-out aquatic exercises with different levels of body immersion.** *J Strength Cond Res* 2007, **21:**1255-1259.4

168. Rahmann AE: **Exercise for people with hip or knee osteoarthritis: a comparison of land-based and aquatic interventions.** *Open Access J Sports Med* 2010, **1:**123-135

169. Raffaelli C, Lanza M, Zanolla L, Zamparo P: **Exercise intensity of head-out water-based activities (water fitness).** *European Journal of Applied Physiology* 2010, **109:**829-838.5

170. Arthritis Foundation: *Arthritis Foundation YMCA Aquatic Program (AFYAP) and AFYAP PLUS Instructor's Guides* 4th edn. Atlanta: The Arthritis Foundation; 2002.

171. Aquatic Exercise Association: *Aquatic Fitness Professional Manual* 5 edn. Nokomis, FL; 2006.

172. Yazigi F, Pinto S, Colado J, Escalante Y, Armada-Da-Silva PA, Brasil R, Alves F: **The cadence and water temperature effect on physiological responses during water cycling.** *Eur J Sport Sci* 2013

173. Barbosa TM, Sousa VF, Silva AJ, Reis VM, Marinho DA, Bragada JA: **Effects of musical cadence in the acute physiologic adaptations to head-out aquatic exercises.** *J Strength Cond Res* 2010, **24:**244-250.1

174. Alberton CL, Tartaruga MP, Pinto SS, Cadore EL, Antunes AH, Finatto P, Kruel LF: **Vertical Ground Reaction Force during Water Exercises Performed at Different Intensities.** *International Journal of Sports Medicine* 2013

175. Barela AM, Stolf SF, Duarte M: **Biomechanical characteristics of adults walking in shallow water and on land.** *J Electromyogr Kinesiol* 2006, **16:**250-256.3

176. Miyoshi T, Shirota T, Yamamoto S, Nakazawa K, Akai M: **Effect of the walking speed to the lower limb joint angular displacements, joint moments and ground reaction forces during walking in water.** *Disabil Rehabil* 2004, **26:**724-732.12

177. Camilotti BM, Rodacki AL, Israel VL, Fowler NE: **Stature recovery after sitting on land and in water.** *Man Ther* 2009

178. Nakazawa K, Yano H, Miyashita M: **Ground reaction forces during walking in water.** *Medicine and Science in Aquatic Sports* 1994, **39:**28-34

179. Alves V: **Exercício Aquático: avaliação das pressões plantares e forças de reacção do apoio.** Faculdade de Motricidade Humana-Universidade Técnica de Lisboa, 2008.

180. Wilcock IM, Cronin JB, Hing WA: **Physiological response to water immersion: a method for sport recovery?** *Sports Med* 2006, **36:**747-765.9

181. Haupenthal A, Fontana HD, Ruschel C, Dos Santos DP, Roesler H: **Ground reaction forces in shallow water running are affected by immersion level, running speed and gender.** *J Sci Med Sport* 2012

182. Poyhonen T, Kyrolainen H, Keskinen KL, Hautala A, Savolainen J, Malkia E: **Electromyographic and kinematic analysis of therapeutic knee exercises under water.** *Clin Biomech (Bristol, Avon)* 2001, **16:**496-504.6

183. Kim IS, Chung SH, Park YJ, Kang HY: **The effectiveness of an aquarobic exercise program for patients with osteoarthritis.** *Appl Nurs Res* 2012, **25:**181-189.3

184. Foley A, Halbert J, Hewitt T, Crotty M: **Does hydrotherapy improve strength and physical function in patients with osteoarthritis--a randomised controlled trial comparing a gym based and a hydrotherapy based strengthening programme.** *Ann Rheum Dis* 2003, **62:**1162-1167.12

185. Gill SD, McBurney H, Schulz DL: **Land-based versus pool-based exercise for people awaiting joint replacement surgery of the hip or knee: results of a randomized controlled trial.** *Arch Phys Med Rehabil* 2009, **90:**388-394.3

186. Lim JY, Tchai E, Jang SN: **Effectiveness of aquatic exercise for obese patients with knee osteoarthritis: a randomized controlled trial.** *PM R* 2010, **2:**723-731; quiz 793.8

187. Messier SP, Legault C, Mihalko S, Miller GD, Loeser RF, DeVita P, Lyles M, Eckstein F, Hunter DJ, Williamson JD, Nicklas BJ: **The Intensive Diet and Exercise for Arthritis (IDEA) trial: design and rationale.** *BMC Musculoskelet Disord* 2009, **10:**93

188. Silva LE, Valim V, Pessanha AP, Oliveira LM, Myamoto S, Jones A, Natour J: **Hydrotherapy versus conventional land-based exercise for the management of patients with osteoarthritis of the knee: a randomized clinical trial.** *Phys Ther* 2008, **88:**12-21.1

189. Wyatt FB, Milam S, Manske RC, Deere R: **The effects of aquatic and traditional exercise programs on persons with knee osteoarthritis.** *J Strength Cond Res* 2001, **15:**337-340.3

190. Thorstensson CA, Roos EM, Petersson IF, Ekdahl C: **Six-week high-intensity exercise program for middle-aged patients with knee osteoarthritis: a randomized controlled trial [ISRCTN20244858].** *BMC Musculoskelet Disord* 2005, **6:**27

191. Cadmus L, Patrick MB, Maciejewski ML, Topolski T, Belza B, Patrick DL: **Community-Based Aquatic Exercise and Quality of Life in Persons with Osteoarthritis.** *Med Sci Sports Exerc* 2010, **42:**8-15.1

192. Bartels EM, Lund H, Hagen KB, Dagfinrud H, Christensen R, Danneskiold-Samsoe B: **Aquatic exercise for the treatment of knee and hip osteoarthritis.** *Cochrane Database Syst Rev* 2007, **17:**CD005523.4

193. Bender T, Karagulle Z, Balint GP, Gutenbrunner C, Balint PV, Sukenik S: **Hydrotherapy, balneotherapy, and spa treatment in pain management.** *Rheumatol Int* 2005, **25:**220-224.3

194. Pais SC: **Aquatic exercise in knee osteoarthritis Patients: effects on symptoms, range of motion, proprioception, strength,function,ground reaction forces and plantar pressures.** *PhD.* Univ de Lisboa, Sports and health; 2007.

195. Hall J, Swinkels A, Briddon J, McCabe CS: **Does aquatic exercise relieve pain in adults with neurologic or musculoskeletal disease? A systematic review and meta-analysis of randomized controlled trials.** *Arch Phys Med Rehabil* 2008, **89:**873-883.5

196. Batterham SI, Heywood S, Keating JL: **Systematic review and meta-analysis comparing land and aquatic exercise for people with hip or knee arthritis on function, mobility and other health outcomes.** *BMC Musculoskelet Disord* 2011, **12:**123

197. Messier SP: **Obesity and osteoarthritis: disease genesis and nonpharmacologic weight management.** *Med Clin North Am* 2009, **93:**145-159, xi-xii.1

198. Hinman RS, Bardin L, Simic M, Bennell KL: **Medial arch supports do not significantly alter the knee adduction moment in people with knee osteoarthritis.** *Osteoarthritis Cartilage* 2013, **21:**28-34.1

199. Altman R, Alarcon G, Appelrouth D, Bloch D, Borenstein D, Brandt K, Brown C, Cooke TD, Daniel W, Feldman D, et al.: **The American College of Rheumatology criteria for the classification and reporting of osteoarthritis of the hip.** *Arthritis Rheum* 1991, **34:**505-514.5

200. Teixeira P, Silva M: *Repensar o PESO: Princípios e Métodos Testados para Controlar o Peso* 2009.

201. Kellgren JH, Lawrence JS: **Radiological assessment of osteo-arthrosis.** *Ann Rheum Dis* 1957, **16:**494-502.4

202. Roos EM, Lohmander LS: **The Knee injury and Osteoarthritis Outcome Score (KOOS): from joint injury to osteoarthritis.** *Health Qual Life Outcomes* 2003, **1:**64

203. Goncalves RS, Cabri J, Pinheiro JP, Ferreira PL: **Cross-cultural adaptation and validation of the Portuguese version of the Knee injury and Osteoarthritis Outcome Score (KOOS).** *Osteoarthritis Cartilage* 2009, **17:**1156-1162.9

204. Turk DC, Dworkin RH, Allen RR, Bellamy N, Brandenburg N, Carr DB, Cleeland C, Dionne R, Farrar JT, Galer BS, et al: **Core outcome domains for chronic pain clinical trials: IMMPACT recommendations.** *Pain* 2003, **106:**337-345.3

205. Mendoza T, Mayne T, Rublee D, Cleeland C: **Reliability and validity of a modified Brief Pain Inventory short form in patients with osteoarthritis.** *Eur J Pain* 2006, **10:**353-361.4

206. Ferreira-Valente MA, Pais Ribeiro JL, Jensen MP: **Further Validation of a Portuguese Version of the Brief Pain Inventory Interference Scale.** *Clínica y Salud* 2012, **23:**89-96

207. Azevedo LF, Pereira AC, Dias C, Agualusa L, Lemos L, Romão J, Castro-Lopes JM: **Tradução, adaptação cultural e estudo multicêntrico de validação de instrumentos para rastreio e avaliação do impacto da dor crónica.** *Dor* 2007, **15:**6-37

208. DGS: **A Dor como 5º sinal vital. Registo sistemático da intensidade da Dor.** (Divisão de Doenças Genéticas CeG ed., vol. 9, DGCG edition. Portugal: DGS; 2003.

209. Beck AT, Steer RA, Ball R, Ranieri W: **Comparison of Beck Depression Inventories -IA and -II in psychiatric outpatients.** *J Pers Assess* 1996, **67:**588-597.3

210. Campos RC, Goncalves B: **The Portuguese Version of the Beck Depression Inventory-II (BDI-II) Preliminary Psychometric Data with Two Nonclinical Samples.** *European Journal of Psychological Assessment* 2011, **27:**258-264.4

211. Beck AT, Steer RA: **Internal consistencies of the original and revised Beck Depression Inventory.** *J Clin Psychol* 1984, **40:**1365-1367.6

212. Brooks D, Solway S, Gibbons WJ: **ATS statement on six-minute walk test.** *Am J Respir Crit Care Med* 2003, **167:**1287.9

213. Goncalves RS, Pinheiro JP, Cabri J: **Evaluation of potentially modifiable physical factors as predictors of health status in knee osteoarthritis patients referred for physical therapy.** *Knee* 2012, **19:**373-379.4

214. Bennell K, Dobson F, Hinman R: **Measures of physical performance assessments: Self-Paced Walk Test (SPWT), Stair Climb Test (SCT), Six-Minute Walk Test (6MWT), Chair Stand Test (CST), Timed Up & Go (TUG), Sock Test, Lift and Carry Test (LCT), and Car Task.** *Arthritis Care Res (Hoboken)* 2011, **63 Suppl 11:**S350-370

215. Enright PL, McBurnie MA, Bittner V, Tracy RP, McNamara R, Arnold A, Newman AB: **The 6-min walk test: a quick measure of functional status in elderly adults.** *Chest* 2003, **123:**387-398.2

216. Rikli RE, Jones CJ: **The development and validation of a functional fitness test for community-residimg older adults. .** *J Aging Phys Act* 1999a, **7:**129-161

217. Bohannon RW: **Sit-to-stand test for measuring performance of lower extremity muscles.** *Percept Mot Skills* 1995, **80:**163-166.1

218. Bohannon RW: **Test-retest reliability of the five-repetition sit-to-stand test: a systematic review of the literature involving adults.** *J Strength Cond Res* 2011, **25:**3205-3207.11

219. Rejeski W, Miller M, Foy C, Messier S, Rapp S: **Self-efficacy and the progression of functional limitations and self-reported disability in older adults with knee pain.** *Journal of Gerontology: Social Sciences* 2001, **56B:**S261-S265.5

220. Rejeski W, Ettinger W, Schumaker S, James P, Burns R, Elam J: **Assessing performance-related disability in patients with knee osteoarthritis.** *Osteoarthritis and Cartilage* 1995, **3:**157-167

221. Rejeski W, Craven T, Ettinger W, McFarlane M, Shumaker S: **Self-efficacy and pain in disability with osteoarthritis of the knee.** *Journal of Gerontology: Psychological Sciences* 1996, **51B:**P24-P29.1

222. Miller M, Rejeski W, Messier S, Loeser R: **Modifiers of change in physical functioning in older adults with knee pain: the observational arthritis study in seniors (OASIS).** *Arthritis Care and Research* 2001, **45:**331-339

223. Messier S, Glasser J, Ettinger W, Craven T, Miller M: **Declines in strength and balance in older adults with chronic knee pain: A 30 month longitudinal, observational study.** *Arthritis & Rheumatism* 2002, **47:**141-148.2

224. Brandt K, Heilman D, Slemenda C, Katz B, Mazzuca S, Braunstein E, Byrd D: **A comparison of lower extremity muscle strength, obesity, and depression scores in elderly subjects with knee pain with and without radiographic evidence of knee osteoarthritis.** *J Rheumatol* 2000, **27:**1937-1946.8

225. Sharma L, Song J, Dunlop D, Felson D, Lewis CE, Segal N, Torner J, Cooke TD, Hietpas J, Lynch J, Nevitt M: **Varus and valgus alignment and incident and progressive knee osteoarthritis.** *Ann Rheum Dis* 2010, **69:**1940-1945.11

226. Barbat-Artigas S, Rolland Y, Zamboni M, Aubertin-Leheudre M: **How to assess functional status: a new muscle quality index.** *J Nutr Health Aging* 2012, **16:**67-77.1

227. Deforche B, Lefevre J, De Bourdeaudhuij I, Hills AP, Duquet W, Bouckaert J: **Physical fitness and physical activity in obese and nonobese Flemish youth.** *Obes Res* 2003, **11:**434-441.3

228. Baptista F, Silva A, Marques E, Mota J, Santos R, Vale S, Ferreira J, Raimundo A, Moreira H: *Observatorio Nacional da Actividade Física e do Desporto: livro verde da aptidão física.* Instituto do Desporto de Portugal (IDP) edn. Lisbon, Portugal: IDP; 2011.

229. Marfell-Jones M, Olds T, Stewart A, Lindsay Carter JE: *International Standards for Anthropometric Assessment. .* Potchefstroom: ISAK.; 2006.

230. Lohman TG, A.F. R, Martorell R: *Anthropometric standardization reference manual.* Champaign, IL: Human Kinetics Publishers; 1998.

231. Craig CL, Marshall AL, Sjostrom M, Bauman AE, Booth ML, Ainsworth BE, Pratt M, Ekelund U, Yngve A, Sallis JF, Oja P: **International physical activity questionnaire: 12-country reliability and validity.** *Med Sci Sports Exerc* 2003, **35:**1381-1395.8

232. Rutten A, Abu-Omar K: **Prevalence of physical activity in the European Union.** *Soz Praventivmed* 2004, **49:**281-289.4

233. Rutten A, Abu-Omar K: **Perceptions of environmental opportunities for physical activity in the European Union.** *Soz Praventivmed* 2004, **49:**310-317.5

234. Lee PH, Macfarlane DJ, Lam TH, Stewart SM: **Validity of the International Physical Activity Questionnaire Short Form (IPAQ-SF): a systematic review.** *Int J Behav Nutr Phys Act* 2011, **8:**115

235. **Guidelines for data processing and analysis of the International Physical Activity Questionnaire (IPAQ)– Short and long forms.** vol. 2006. www.ipaq.ki.se.; 2005.

236. Hurst H, Bolton J: **Assessing the clinical significance of change scores recorded on subjective outcome measures.** *J Manipulative Physiol Ther* 2004, **27:**26-35.1

237. Taylor R: **Interpretation of the correlation coefficient: a basic review.** *Journal of Diagnostic Medical Sonography* 1990, **6:**35-39.January

238. Cohen J: *Statistical power analysis for the behavioral sciences.* 2nd edn. Hillsdale, NJ: Lawrence Erlbaum Associates; 1998.

239. Ahmad CS, Clark AM, Heilmann N, Schoeb JS, Gardner TR, Levine WN: **Effect of gender and maturity on quadriceps-to-hamstring strength ratio and anterior cruciate ligament laxity.** *Am J Sports Med* 2006, **34:**370-374.3

240. Coombs R, Garbutt G: **Developments in the Use of the Hamstring/Quadriceps Ratio for the Assessment of Muscle Balance.** *J Sports Sci Med* 2002, **1:**56-62.3

241. Jakobi JM, Chilibeck PD: **Bilateral and unilateral contractions: possible differences in maximal voluntary force.** *Can J Appl Physiol* 2001, **26:**12-33.1

242. Kvist J: **Rehabilitation following anterior cruciate ligament injury: current recommendations for sports participation.** *Sports Med* 2004, **34:**269-280.4

243. Alnahdi AH, Zeni JA, Snyder-Mackler L: **Muscle impairments in patients with knee osteoarthritis.** *Sports Health* 2012, **4:**284-292.4

244. Amin S, Baker K, Niu J, Clancy M, Goggins J, Guermazi A, Grigoryan M, Hunter DJ, Felson DT: **Quadriceps strength and the risk of cartilage loss and symptom progression in knee osteoarthritis.** *Arthritis Rheum* 2009, **60:**189-198.1

245. Fischer SL, Grewal TJ, Wells R, Dickerson CR: **Effect of bilateral versus unilateral exertion tests on maximum voluntary activity and within-participant reproducibility in the shoulder.** *J Electromyogr Kinesiol* 2011, **21:**311-317.2

246. Becker BE: **Aquatic therapy: scientific foundations and clinical rehabilitation applications.** *PM R* 2009, **1:**859-872.9

247. Hartmann S, Huch R: **Response of pregnancy leg edema to a single immersion exercise session.** *Acta Obstet Gynecol Scand* 2005, **84:**1150-1153.12

248. Onodera S, Miyachi M, Nishimura M, Yamamoto K, Yamaguchi H, Takahashi K, In JY, Amaoka H, Yoshioka A, Matsui T, Hara H: **Effects of water depth on abdominal [correction of abdominails] aorta and inferior vena cava during standing in water.** *J Gravit Physiol* 2001, **8:**P59-60.1

249. Maly MR, Costigan PA, Olney SJ: **Contribution of psychosocial and mechanical variables to physical performance measures in knee osteoarthritis.** *Phys Ther* 2005, **85:**1318-1328.12

250. Segal NA, Torner JC, Felson D, Niu J, Sharma L, Lewis CE, Nevitt M: **Effect of thigh strength on incident radiographic and symptomatic knee osteoarthritis in a longitudinal cohort.** *Arthritis Rheum* 2009, **61:**1210-1217.9

251. Aagaard P, Simonsen EB, Trolle M, Bangsbo J, Klausen K: **Isokinetic hamstring/quadriceps strength ratio: influence from joint angular velocity, gravity correction and contraction mode.** *Acta Physiol Scand* 1995, **154:**421-427.4

252. Hewett TE, Myer GD, Zazulak BT: **Hamstrings to quadriceps peak torque ratios diverge between sexes with increasing isokinetic angular velocity.** *J Sci Med Sport* 2008, **11:**452-459.5

253. Aagaard P, Simonsen EB, Magnusson SP, Larsson B, Dyhre-Poulsen P: **A new concept for isokinetic hamstring: quadriceps muscle strength ratio.** *Am J Sports Med* 1998, **26:**231-237.2

254. Fitzgerald GK, Piva SR, Irrgang JJ, Bouzubar F, Starz TW: **Quadriceps activation failure as a moderator of the relationship between quadriceps strength and physical function in individuals with knee osteoarthritis.** *Arthritis Rheum* 2004, **51:**40-48.1

Appendices

Documents and publications which were considered relevant for the this study understanding were included. Firstly are the questionnaires and documents related to the methods chapters and secondly are presented publications related to this dissertation.

Appendix 1: Tests list of PICO Project

Tests list of the PICO project

ASSESSMENT/TESTS	Pre-screening	Baseline	3 months
Questionnaires			
Interview	x		
KOPS	x		x
IPAQ		x	x
KOOS		x	x
Beck Depression Inventory		x	x
Weight andLifestyle inventory		x	x
Brief Pain Inventory		x	x
Physical Function			
6MWT		x	x
Knee Strength		x	x
Hand Grip Strength		x	x
Flexibility		x	x
Gait Analysis		x	x
Morphology and Body Composition			
Anthropometry		x	x
Fat mass and BMD (DXA scan)		x	x
Radiology			
Knee X-ray (Lateral and A-P)	x		

Appendix 2: Informed consent

PROJECTO PICO

Informação e Consentimento informado

Está a ser convidado(a) a participar num projecto de investigação que pretende estudar os efeitos de um programa de intervenção na Osteoartrose do joelho. A selecção para a participação baseia-se nos critérios de elegibilidade do estudo (ter mais que 40 anos de idade, ter sobrepeso ou obesidade e não estar a frequentar nenhum programa formal de exercícios) e no diagnóstico de Osteoartrose no joelho, confirmado por exame radiológico e pela análise do questionário respondido anteriormente.

No caso de confirmação de diagnóstico, após a realização do raio X, o participante compromete-se através deste documento a continuar a sua participação no estudo. A aceitação na participação deste projecto implica um compromisso mútuo no cumprimento dos seguintes aspectos.

1. Como participante será integrado aleatoriamente num dos dois grupos de intervenção:

    - Grupo 1: Será submetido a um programa de exercício aquático durante três meses (Março, Abril, Maio), duas vezes por semana, no Concelho de Oeiras, Lisboa ou de Setúbal. Poderá escolher o local consoante a sua conveniência. Se ficar no programa de exercício terá de assinar um termo de responsabilidade imposto pelo local de realização das sessões práticas.

    - Grupo 2: Será submetido a um programa educacional oferecido pelo programa **Peso Comunitário**. Constará numa sessão por semana com hora prevista às 18.00h na Faculdade de Motricidade Humana (FMH). Este programa iniciar-se-á em Março e terá a duração de três meses. No caso de fazer parte deste grupo, depois do programa educacional, poderá existir a oportunidade de num programa de exercício aquático.

2. Todos os participantes terão de realizar testes de aptidão física e do estado de saúde em geral antes do início do programa de intervenção e imediatamente após o seu término. De maneira a não sobrecarregar os participantes os testes estarão organizados em dois dias distintos, pelo que deverá se deslocar à FMH duas vezes no período de 15 de Janeiro e 28 de Fevereiro e duas vezes no período de 1 de Junho-30 de Junho. Todos os testes serão realizados por profissionais especializados e de acordo com as normas científicas.

3. Os custos do programa e dos testes serão suportados pelo projecto, excepto o seguro de acidentes pessoais que ficará ao encargo de cada participante, pelo valor de 5€ (período de cobertura de 15 de Janeiro - 30 de Junho).

4. A informação obtida neste estudo é confidencial e não será revelada a pessoa alguma sem o seu consentimento prévio, excepto à equipa responsável pelo estudo.

5. A equipa do PICO compromete-se a entregar a cada participante um relatório geral com a informação da aptidão física antes e após o período de intervenção.

Em caso de dúvida ou de necessidade de informações adicionais poderá contactar a equipa do **Projecto PICO** a partir do telefone **924155372** Também poderá utilizar o seguinte correio electrónico: **pico@fmh.utl.pt**

A sua colaboração é imprescindível para o aprofundamento do conhecimento nesta área.
Obrigada pela disponibilidade!

Faculdade de Motricidade Humana

Informação e Consentimento informado

Consentimento Informado

1. Declaro que li as informações no texto acima e que me foram explicados os objectivos da participação no projecto PICO.
2. Declaro que me foi entregue a documentação anexa com a explicação sobre os testes a serem realizados.
3. Comprometo-me a cumprir o calendário proposto.
4. Sei que não é me devida qualquer compensação monetária pela participação no projecto PICO.
5. Aceito que os resultados deste estudo possam ser divulgados ou publicados, mas o meu nome ou identidade não serão revelados sem a minha autorização. Os meus dados são confidenciais.

Nome completo:____

Data: ____ de ___________ de 20______ ___________________________________

Assinatura

Declaro que são verdadeiras todas as afirmações aqui descritas.

Flávia Giovanetti Yázigi (Responsável do estudo)

Appendix 3: Aquatic Exercise Patterns

LOWER BODY STRENGHT EXERCISES

1

2

Unilateral Hip abduction followed of knee extension/flexion

1

2

Hip flexion: Knee flexion extension

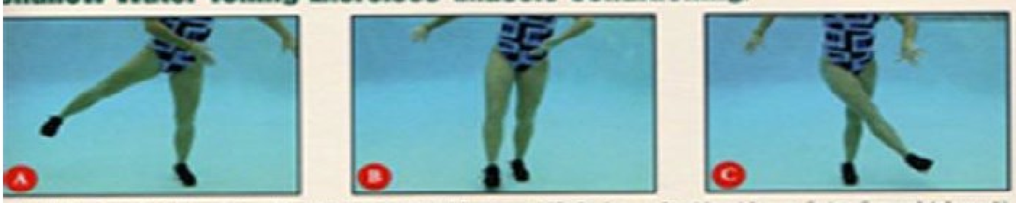
Hip flexion/extension | Knee flexion/ extension

1

2

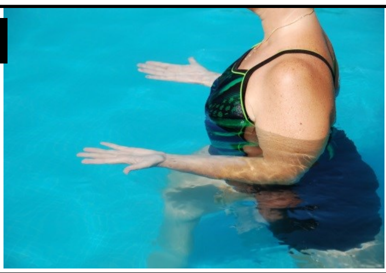
Hip flexion/extension with external rotation

Shallow Water Toning Exercises (Muscle Conditioning)

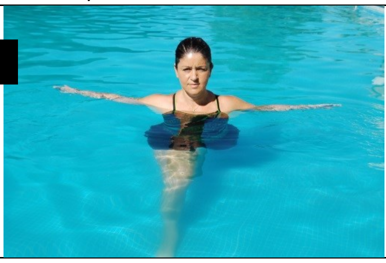


Hip Abduction & Adduction – Hip Abductors & Adductors: Lift the leg to the side with toes facing forward (photo A) and pull back down to center (photo B). Crossing the midline is acceptable (photo C) unless participant has had hip replacement surgery.

1




Elbow flexion/extension

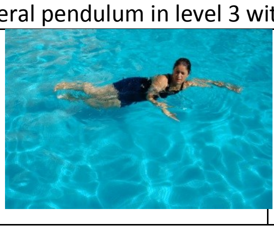



Shoulder horizontal adduction/abduction


Shoulder adduction/abduction with forearm in pronation




ABS: Antero- posterior bilateral pendulum in level 3 with bounce in the center

ABS: Lateral pendulum in level 3 combined with bounce in the center

Appendix 4: Knee Osteoarthritis Pre- Screening Questionnaire (KOPS)

Epidemiologia da Osteoartrose – Projecto PICO

Neuromechanics

Cod:

QUESTIONÁRIO

Nome:____

Telefone: __________________ E-mail:_________________________________

Morada:____

Freguesia:_________________Concelho*:___________________________ Cod. Postal:________-_________

Data de Nascimento*: _______/________/_______ Sexo* F [ ] M [ ]

Escolaridade*:_____________ Profissão atual ou a que se dedicou a maior parte da vida*:_________________

Se for reformado(a), indique a idade com que se reformou*: _________ Estado Civil*:_____________________

Se está na menopausa, indique a idade de início*:______ Altura*:________ cm Peso*: ________ Kg

Há quanto tempo tem este peso?* Há menos que 5 anos [ ] Entre 5-10 anos [ ] Há mais que 10 anos [ ] Não sei [ ]

*Os campos assinalados são de preenchimento obrigatório; os campos referentes ao nome, contacto e morada são importantes no caso de pretender ser contactado para participação em programas de exercício ou educacional que possam vir a ser realizados.

1. **Já alguma vez teve dor persistente ou repetitiva não associada a um traumatismo em alguma articulação?**

   [ ] Não [ ] Sim

   1.1. Se respondeu sim, assinale o(s) local(is) onde costuma sentir dor:

Coluna cervical (Pescoço)	[ ]	Ombro	[ ]	Anca	[ ]
Coluna dorsal (Costas)	[ ]	Cotovelo	[ ]	Joelho	[ ]
Coluna lombar	[ ]	Mão	[ ]	Tornozelo	[ ]

2. **O seu médico já lhe diagnosticou Osteoartrose (Artrose)?** [ ] Não [ ] Sim [ ] Não sei

   2.1. Se respondeu sim, assinale com um "x" a(s) região(ões) que tem diagnóstico de Osteoartrose.

Coluna cervical (Pescoço)	[ ]	Ombro	[ ]	Anca	[ ]
Coluna dorsal (Costas)	[ ]	Cotovelo	[ ]	Joelho	[ ]
Coluna lombar	[ ]	Mão	[ ]	Tornozelo	[ ]

   2.2. Se assinalou que tem Osteoartrose no joelho, indique há quantos anos:________

3. **Já sofreu alguma fractura, intervenção cirúrgica ou lesão grave no(s) membro(s) inferior(es) que o obrigasse a afastar-se temporariamente das suas actividades diárias (trabalho, desporto, etc...)?** [ ] Não [ ] Sim

   3.1. Se respondeu sim, preencha o quadro com o tipo, membro lesionado e ano de ocorrência:

Tipo de lesão ou cirurgia nos membros inferiores	Membro	Ano
1º		
2º		

3.2. Se respondeu sim, refira durante quanto tempo esteve afastado das suas actividades diárias após a lesão reportada?

Tempo de afastamento	1ª Lesão	2ª Lesão
Menos do que 1 semana		
Mais do que 1 semana		
Mais do que 15 dias		
Mais do que 1 mês		
Mais do que 3 meses		

4. Exerce ou exerceu alguma(s) profissão(ões) em que permaneça muitas horas em pé, sentado ou agachado?

☐ Não ☐ Sim

4.1. Se sim, qual(is) ?____

Predominantemente em pé ☐ Predominantemente sentado ☐

Predominantemente agachado ☐ Todas as anteriores ☐

5. Pratica ou praticou algum(ns) desporto(s) regularmente (futebol, voleibol, ténis, natação, basquetebol, andebol, atletismo, ciclismo, hóquei, ginástica desportiva, corrida ou outro)? ☐ Não ☐ Sim

5.1. Se sim, preencha o quadro com o desporto que praticou:

Desporto	Anos de prática	Frequência semanal (média)	Foi federado?

6. Costuma sentir dor no Joelho? ☐ Não ☐ Sim ☐ Às vezes

6.1. Se respondeu sim na questão 6, assinale qual (is) o(s) joelho(s) em que sentiu ou sente mais dor?

☐ Direito ☐ Esquerdo ☐ Ambos

6.2. Se respondeu sim na questão 6, escolha <u>uma ou mais</u> afirmações que melhor represente o caso dos seus joelhos:

☐ Durante o último ano teve mais de três episódios de dor. Considera-se "episódio de dor" a situação de dor intensa que pode durar horas ou dias, desaparecendo depois completamente (marque um "X" sobre o número que corresponde a máxima intensidade da dor que sentiu).

Sem Dor	0	1	2	3	4	5	6	7	8	9	10	Dor Máxima

☐ Durante os últimos seis meses pelo menos uma vez a dor durou mais que uma semana.

☐ Durante o último mês teve dor (marque um "X" sobre o número que corresponda a máxima intensidade da dor que sentiu).

Sem Dor	0	1	2	3	4	5	6	7	8	9	10	Dor Máxima

7. Sentiu no último mês, dor no(s) joelho(s) em alguma destas situações? (Assinale com "x" a intensidade da dor)

7.1. Ao caminhar ☐ Não ☐ Sim

Sem Dor	0	1	2	3	4	5	6	7	8	9	10	Dor Máxima

7.2. Ao subir/descer escadas ou rampas? ☐ Não ☐ Sim

Sem Dor	0	1	2	3	4	5	6	7	8	9	10	Dor Máxima

7.3. Ao levantar-se da cadeira? ☐ Não ☐ Sim

Sem Dor	0	1	2	3	4	5	6	7	8	9	10	Dor Máxima

7.4. Ao manter-se de pé? ☐ Não ☐ Sim

Sem Dor	0	1	2	3	4	5	6	7	8	9	10	Dor Máxima

8. Sente dificuldade em realizar alguma(s) das tarefas abaixo citadas? ☐ Não ☐ Sim

8.1. Se sim, assinale aqueles que mais sente dificuldade em realizar:

Caminhar ☐ Levantar-se ☐ Subir/Descer escada ☐ Manter-se de pé ☐

9. Rigidez é uma sensação de dificuldade em iniciar o movimento (sensação de articulação presa). Sentiu no último mês, rigidez no(s) joelho(s) de manhã ao acordar com duração inferior a 30 minutos?

☐ Não ☐ Sim ☐ Às vezes

10. Sentiu no último mês, rigidez no(s) joelho(s) depois de estar muito tempo sentado(a) ou em pé?

☐ Não ☐ Sim ☐ Às vezes

11. Teve no último mês, o(s) joelho(s) inchado(s) ?

☐ Não ☐ Sim ☐ Às vezes

12. No último mês sentiu ou ouviu o(s) seu(s) joelho(s) ranger, crepitar (pequenos ressaltos) ou a fazer estalos quando se movimenta ou se dobra? ☐ Não ☐ Sim ☐ Às vezes

13. Consegue fazer a extensão completa do(s) seu(s)joelho(s) (mantê-los esticados quando está deitado ou sentado sem apoio)? ☐ Não ☐ Sim ☐ Às vezes

14. Considera-se um joelho deformado quando este apresenta uma alteração no seu aspecto (formato diferente do normal que não deve ser confundido com inchaço temporário).
Tem algum dos joelhos deformado? ☐ Não ☐ Sim ☐ Não sei

14.1. Se sim, qual(is)? ☐ Direito ☐ Esquerdo

SE RESPONDEU <u>SIM</u> EM ALGUMA DAS QUESTÕES SOBRE SINTOMAS NO SEU JOELHO(6-14), RESPONDA AS QUESTÕES 15-16; SE RESPONDEU <u>NÃO,</u> SALTE PARA A QUESTÃO 17.

15. No último ano procurou o médico por causa desses sintomas acima referidos (dor, rigidez ou inchaço) tendo-lhe sido prescritos exames ou tratamento? ☐ Não ☐ Sim

16. Está a tomar algum medicamento para o alívio da dor no(s) seu(s) joelho(s)? ☐ Não ☐ Sim

16.1. Se sim, qual? ☐ Anti-inflamatório ☐ Analgésico ☐ Outro ☐ Não sei

Dor Máxima

Devido ao seu problema no(s) joelho(s) utiliza algum equipamento para o auxílio da marcha? ☐ Não ☐ Sim

16.2. Se sim, qual? Canadiana ☐ Bengala ☐ Andarilho ☐ Outro ☐

17. Está a frequentar algum programa de exercício (ginástica, hidroginástica, manutenção, musculação, etc.)?

☐ Não ☐ Sim Se sim, qual? _________________ Quantas vezes por semana?_______

Appendix 5: Knee injury and Osteoarthritis Outcome Score (**KOOS**)

QUESTIONÁRIO KOOS SOBRE O JOELHO

Data: _____/______/______ Data de nascimento: _____/______/______

Nome: ____

INSTRUÇÕES: Este questionário pretende saber como vê o seu joelho. Esta informação dar-nos-á dados sobre como se sente em relação ao joelho e até que ponto é que é capaz de desempenhar as suas actividades normais.
Responda a cada uma das perguntas marcando o quadrado adequado, apenas um quadrado para cada pergunta. Se não tiver a certeza sobre a resposta a escolher, por favor escolha a que achar melhor.

Sintomas
Estas perguntas devem ser respondidas tendo em conta os sintomas no seu joelho durante a **última semana**.

S1. Tem tido o joelho inchado?

Nunca	Raramente	Às vezes	Frequentemente	Sempre
☐	☐	☐	☐	☐

S2. Tem sentido ranger, ouvido um estalo ou qualquer outro som quando mexe o joelho?

Nunca	Raramente	Às vezes	Frequentemente	Sempre
☐	☐	☐	☐	☐

S3. Tem sentido o joelho preso ou bloqueado quando se mexe?

Nunca	Raramente	Às vezes	Frequentemente	Sempre
☐	☐	☐	☐	☐

S4. Tem conseguido esticar o joelho completamente?

Sempre	Frequentemente	Às vezes	Raramente	Nunca
☐	☐	☐	☐	☐

S5. Tem conseguido dobrar o joelho completamente?

Sempre	Frequentemente	Às vezes	Raramente	Nunca
☐	☐	☐	☐	☐

Rigidez
As perguntas que se seguem dizem respeito ao grau de rigidez no joelho que teve na **última semana**. Rigidez é uma sensação de dificuldade ou lentidão a mexer o seu joelho.

S6. Até que ponto sente rigidez no joelho logo após acordar de manhã?

Nada	Pouco	Moderadamente	Muito	Muitíssimo
☐	☐	☐	☐	☐

S7. Até que ponto sente rigidez no joelho depois de se sentar, deitar ou descansar **ao fim do dia**?

Nada	Pouco	Moderadamente	Muito	Muitíssimo
☐	☐	☐	☐	☐

Dor

P1. Com que frequência tem dores no joelho?

Nunca	Uma vez por mês	Uma vez por semana	Todos os dias	Sempre
☐	☐	☐	☐	☐

Que intensidade de dor no joelho é que teve durante a **última semana** nas seguintes actividades?

P2. Rodar/virar-se/torcer sobre o joelho

Nenhuma	Pouca	Moderada	Muita	Muitíssima
☐	☐	☐	☐	☐

P3. Esticar o joelho completamente

Nenhuma	Pouca	Moderada	Muita	Muitíssima
☐	☐	☐	☐	☐

P4. Dobrar o joelho completamente

Nenhuma	Pouca	Moderada	Muita	Muitíssima
☐	☐	☐	☐	☐

P5. Andar sobre uma superfície plana

Nenhuma	Pouca	Moderada	Muita	Muitíssima
☐	☐	☐	☐	☐

P6. Subir ou descer escadas

Nenhuma	Pouca	Moderada	Muita	Muitíssima
☐	☐	☐	☐	☐

P7. À noite, na cama

Nenhuma	Pouca	Moderada	Muita	Muitíssima
☐	☐	☐	☐	☐

P8. Estar sentado/a ou deitado/a

Nenhuma	Pouca	Moderada	Muita	Muitíssima
☐	☐	☐	☐	☐

P9. Estar de pé

Nenhuma	Pouca	Moderada	Muita	Muitíssima
☐	☐	☐	☐	☐

Actividades da vida diária

As perguntas que se seguem dizem respeito à sua função física. Por função física referimo-nos à sua capacidade de se deslocar e de cuidar de si. Para cada uma das actividades seguintes, indique o grau de dificuldade que sentiu na **última semana** por causa do seu joelho.

A1. Descer escadas

Nenhuma	Pouca	Moderada	Muita	Muitíssima
☐	☐	☐	☐	☐

A2. Subir escadas

Nenhuma	Pouca	Moderada	Muita	Muitíssima
☐	☐	☐	☐	☐

Para cada uma das seguintes actividades indique, por favor, o grau de dificuldade que teve na última semana devido ao seu joelho.

A3. Levantar-se a partir da posição de sentado/a

Nenhuma	Pouca	Moderada	Muita	Muitíssima
☐	☐	☐	☐	☐

A4. Manter-se de pé

Nenhuma	Pouca	Moderada	Muita	Muitíssima
☐	☐	☐	☐	☐

A5. Dobrar-se para baixo/apanhar um objecto

Nenhuma	Pouca	Moderada	Muita	Muitíssima
☐	☐	☐	☐	☐

A6. Andar numa superfície plana

Nenhuma	Pouca	Moderada	Muita	Muitíssima
☐	☐	☐	☐	☐

A7. Entrar ou sair do carro

Nenhuma	Pouca	Moderada	Muita	Muitíssima
☐	☐	☐	☐	☐

A8. Ir às compras

Nenhuma	Pouca	Moderada	Muita	Muitíssima
☐	☐	☐	☐	☐

A9. Calçar meias/collants

Nenhuma	Pouca	Moderada	Muita	Muitíssima
☐	☐	☐	☐	☐

A10. Levantar-se da cama

Nenhuma	Pouca	Moderada	Muita	Muitíssima
☐	☐	☐	☐	☐

A11. Descalçar meias/collants

Nenhuma	Pouca	Moderada	Muita	Muitíssima
☐	☐	☐	☐	☐

A12. Estar deitado/a na cama (virar-se, manter a posição do joelho)

Nenhuma	Pouca	Moderada	Muita	Muitíssima
☐	☐	☐	☐	☐

A13. Entrar/sair da banheira

Nenhuma	Pouca	Moderada	Muita	Muitíssima
☐	☐	☐	☐	☐

A14. Estar sentado/a

Nenhuma	Pouca	Moderada	Muita	Muitíssima
☐	☐	☐	☐	☐

A15. Sentar-se ou levantar-se da sanita

Nenhuma	Pouca	Moderada	Muita	Muitíssima
☐	☐	☐	☐	☐

Para cada uma das actividades seguintes, indique o grau de dificuldade que sentiu na **última semana** por causa do seu joelho.

A16. Tarefas domésticas pesadas (ex.: pegar em caixas pesadas, esfregar o chão, etc.)

Nenhuma	Pouca	Moderada	Muita	Muitíssima
☐	☐	☐	☐	☐

A17. Tarefas domésticas leves (ex.: cozinhar, limpar o pó, etc.)

Nenhuma	Pouca	Moderada	Muita	Muitíssima
☐	☐	☐	☐	☐

Actividades desportivas e de lazer

As perguntas que se seguem dizem respeito à sua função física, estando activo/a a um nível mais elevado. As perguntas devem ser respondidas tendo em conta o grau de dificuldade que teve durante a **última semana** por causa do seu joelho.

SP1. Pôr-se de cócoras

Nenhuma	Pouca	Moderada	Muita	Muitíssima
☐	☐	☐	☐	☐

SP2. Correr

Nenhuma	Pouca	Moderada	Muita	Muitíssima
☐	☐	☐	☐	☐

SP3. Saltar

Nenhuma	Pouca	Moderada	Muita	Muitíssima
☐	☐	☐	☐	☐

SP4. Rodar/virar-se/torcer sobre o joelho afectado

Nenhuma	Pouca	Moderada	Muita	Muitíssima
☐	☐	☐	☐	☐

SP5. Ajoelhar

Nenhuma	Pouca	Moderada	Muita	Muitíssima
☐	☐	☐	☐	☐

Qualidade de Vida

Q1. Com que frequência é que tem consciência do problema que tem no joelho?

Nunca	Uma vez por mês	Uma vez por semana	Todos os dias	Constantemente
☐	☐	☐	☐	☐

Q2. Modificou o seu estilo de vida para evitar actividades que poderiam afectar o joelho?

De modo algum	Um pouco	Moderadamente	Muito	Completamente
☐	☐	☐	☐	☐

Q3. Até que ponto é que a falta de confiança no joelho o/a incomoda?

Nada	Um pouco	Moderadamente	Muito	Muitíssimo
☐	☐	☐	☐	☐

Q4. Em geral, o joelho causa-lhe muitos problemas?

Nenhuns	Poucos	Alguns	Muitos	Muitíssimos
☐	☐	☐	☐	☐

Obrigado por ter respondido a todas as perguntas do questionário.

Appendix 6: Brief Pain Inventory (short version)

STUDY ID#:__________ DO NOT WRITE ABOVE THIS LINE HOSPITAL #:__________

Inventário Resumido da Dor (Formulário Abreviado)

Data: ___/ ___/ ___ **Hora:** __________

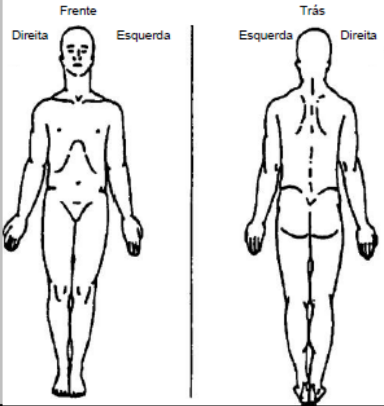
Nome: __________________ __________________

Apelido Nome próprio

1. Ao longo da vida, a maior parte de nós teve dor de vez em quando (tais como dores de cabeça de pequena importância, entorses e dores de dentes). Teve alguma dor diferente destas dores comuns hoje?

1. Sim 2. Não

2. Nas figuras marque as áreas onde sente dor. Coloque um X na zona que lhe dói mais.



3. Por favor, classifique a sua dor assinalando com um círculo o número que melhor descreve a sua dor no seu máximo nas últimas 24 horas.

0	1	2	3	4	5	6	7	8	9	10
Sem dor										A pior dor que se pode imaginar

4. Por favor, classifique a sua dor assinalando com um círculo o número que melhor descreve a sua dor no seu mínimo nas últimas 24 horas.

0	1	2	3	4	5	6	7	8	9	10
Sem dor										A pior dor que se pode imaginar

5. Por favor, classifique a sua dor assinalando com um círculo o número que melhor descreve a sua dor em média.

0	1	2	3	4	5	6	7	8	9	10
Sem dor										A pior dor que se pode imaginar

6. Por favor classifique a sua dor assinalando com um círculo o número que indica a intensidade da sua dor neste preciso momento.

0	1	2	3	4	5	6	7	8	9	10
Sem dor										A pior dor que se pode imaginar

Página 1 de 2

BPI-SF - Portugal/Portuguese - June 18, 2007

STUDY ID#: __________ DO NOT WRITE ABOVE THIS LINE HOSPITAL#: __________

Data: ___/___/___ Hora: ______

Nome: ____________________ ____________________

Apelido Nome próprio

7. Que tratamentos ou medicamentos está a fazer para a sua dor?

____

____

8. Nas últimas 24 horas, até que ponto é que os tratamentos e os medicamentos aliviaram a sua dor? Por favor, assinale com um círculo a percentagem que melhor demonstra o alívio que sentiu.

0%	10%	20%	30%	40%	50%	60%	70%	80%	90%	100%
Nenhum alívio										Alívio completo

9. Assinale com um círculo o número que descreve em que medida é que, durante as últimas 24 horas, a sua dor interferiu com a sua/seu:

A. Actividade geral

0	1	2	3	4	5	6	7	8	9	10
Não interferiu										Interferiu completamente

B. Disposição

0	1	2	3	4	5	6	7	8	9	10
Não interferiu										Interferiu completamente

C. Capacidade para andar a pé

0	1	2	3	4	5	6	7	8	9	10
Não interferiu										Interferiu completamente

D. Trabalho normal (inclui tanto o trabalho doméstico como o trabalho fora de casa)

0	1	2	3	4	5	6	7	8	9	10
Não interferiu										Interferiu completamente

E. Relações com outras pessoas

0	1	2	3	4	5	6	7	8	9	10
Não interferiu										Interferiu completamente

F. Sono

0	1	2	3	4	5	6	7	8	9	10
Não interferiu										Interferiu completamente

G. Prazer de viver

0	1	2	3	4	5	6	7	8	9	10
Não interferiu										Interferiu completamente

BPI-SF - Portugal/Portuguese - June 18, 2007

Appendix 7: Beck Depression Inventory II

A preencher pela equipa PICO

Momento de Avaliação □□ Nome:______________________________________
Data □□/□□/□□ N.º da participante: □□□□ Grupo: □
Introdução □□□ (Iniciais) Data Preenchimento: □□/□□/□□ (mês / dia / ano)

IDB II

Este questionário é composto por 21 grupos de afirmações. Por favor leia cada grupo de afirmações cuidadosamente e depois escolha **uma afirmação**, em cada grupo, que melhor descreva a forma como se tem sentido nas **duas últimas semanas, incluindo o dia de hoje.** Faça um círculo à volta do número correspondente à afirmação que seleccionou. Se lhe parecer que diversas frases do mesmo grupo se aplicam igualmente bem, coloque o círculo à volta do número mais elevado para esse grupo. Assegure-se de que não escolhe mais do que uma frase em cada grupo, inclusive no Item 16 (Mudanças no Padrão de Sono) ou no Item 18 (Mudanças no Apetite).

1. Tristeza
Não me sinto triste 0
Sinto-me triste a maior parte do tempo 1
Estou sempre triste 2
Estou tão triste ou infeliz que não aguento mais 3

2. Pessimismo
Não estou pessimista em relação ao meu futuro 0
Sinto-me mais pessimista acerca do meu futuro do que era normal 1
Não espero que as coisas se vão resolver em meu benefício 2
Não tenho esperança no meu futuro e penso que ainda irá piorar 3

3. Fracassos do passado
Não me sinto um falhado/a 0
Fracassei mais do que deveria 1
Quando olho para o meu passado, vejo imensos fracassos 2
Como pessoa, sinto-me completamente falhado/a 3

4. Perda de prazer
Sinto a mesma satisfação de sempre, com as coisas de que gosto 0
Não gosto tanto das coisas como gostava antes 1
Obtenho muito pouco prazer das coisas de que costumava gostar 2
Não consigo ter qualquer prazer com as coisas de que costumava gostar 3

5. Sentimentos de culpa
Não me sinto particularmente culpado/a 0
Sinto-me culpado/a com muitas coisas que fiz ou que devia ter feito 1
Sinto-me culpado/a a maior parte do tempo 2
Sinto-me constantemente culpado/a 3

6. Sentimentos de punição
Não sinto que esteja a ser punido/a 0
Sinto que talvez venha a ser punido/a 1
Espero vir a ser punido/a 2
Sinto que estou a ser punido/a 3

7. Auto-desvalorização
O que sinto acerca de mim próprio/a não se tem alterado 0
Perdi a confiança em mim 1
Estou desiludido comigo próprio/a 2
Não gosto de mim 3

8. Auto-crítica
Não me critico ou culpo mais do que o habitual 0
Sou mais crítico/a de mim próprio/a do que era habitual 1
Critico-me por todos os meus erros 2
Culpo-me por todo o mal que acontece 3

9. Pensamentos ou desejos suicidas
Não tenho pensamentos suicidas 0
Tenho pensamentos suicidas, mas nunca os levaria à prática 1
Gostaria de me suicidar 2
Se tivesse oportunidade matava-me 3

10. Chorar
Não choro mais do que chorava 0
Choro mais do que costumava chorar 1
Choro por tudo e por nada 2
Tenho vontade de chorar mas não consigo 3

11. Agitação
Não estou mais inquieto/a ou agitado/a do que o normal 0
Sinto-me mais inquieto/a ou agitado/a do que o normal......1
Estou tão inquieto/a ou agitado/a que é difícil ficar parado/a......2
Estou tão inquieto/a ou agitado/a que tenho de estar sempre a mexer-me ou a fazer alguma coisa......3

12. Perda de interesse
Não perdi o interesse nas outras pessoas ou actividades 0
Estou menos interessado nas outras pessoas ou coisas do que era habitual......1
Perdi a maior parte do interesse nas outras pessoas ou coisas 2
É muito difícil interessar-me por alguma coisa......3

13. Indecisão
Tomo decisões tão bem como sempre......0
Sinto mais dificuldade em tomar decisões do que é normal......1
Tenho muito mais dificuldade em tomar decisões do que antes......2
Tenho problemas em tomar qualquer decisão 3

14. Sentimento de inutilidade
Não sinto que seja um/uma inútil ou uma pessoa sem valor 0
Não considero que tenha tanto valor e utilidade como dantes......1
Sinto que tenho menos valor quando me comparo com outras pessoas......2
Sinto-me completamente inútil e sem valor 3

15. Perda de energia
Tenho tanta energia como sempre......0
Tenho menos energia do que era habitual......1
Não tenho energia para fazer muita coisa......2
Não tenho energia para o que quer que seja 3

16. Alterações no ritmo de sono
Não tenho notado qualquer mudança no meu padrão de sono......0
Durmo um pouco mais/menos do que o costume......1
OU
Durmo muito mais/menos do que o costume 2
Durmo a maior parte do dia 3
Acordo 1-2 horas mais cedo e não consigo voltar a adormecer......3

17. Irritabilidade
Não estou mais irritável do que o normal......0
Estou mais irritável do que o normal......1
Estou muito mais irritável do que o normal 2
Estou sempre irritável 3

18. Mudanças no apetite
Não noto qualquer mudança no meu apetite 0
O meu apetite é um pouco menor do que o normal......1
OU
O meu apetite é um pouco maior do que o normal......1
O meu apetite é muito menor do que antes 2
OU
O meu apetite é muito maior do que antes 2
Não tenho nenhum apetite......3
Estou constantemente com vontade de comer 3

19. Dificuldade de concentração
Consigo-me concentrar tão bem como sempre......0
Não me consigo concentrar tão bem como o habitual 1
É difícil concentrar-me nalguma coisa durante muito tempo 2
Acho que não me consigo concentrar em nada 3

20. Cansaço ou falta de energia
Não me sinto mais cansado ou sem energia do que o normal......0
Fico cansado ou sem energia mais facilmente do que o normal 1
Sinto-me demasiado cansado ou sem energia para fazer muitas das coisas que costumava fazer 2
Sinto-me demasiado cansado ou sem energia para fazer a maior parte das coisas que costumava fazer 3

21. Perda de interesse em sexo
Não notei qualquer mudança recente no meu interesse por sexo......0
Tenho menos interesse por sexo do que era habitual......1
Actualmente estou muito menos interessado em sexo......2
Perdi completamente o interesse por sexo......3

Appendix 8: Physical Activity Questionnaire (IPAQ)

QUESTIONARIO INTERNACIONAL DE AVALIAÇAO DA ACTIVIDADE FÍSICA - IPAQ- Versão Portuguesa Curta *

Este questionário inclui questões sobre a actividade física que realiza habitualmente para se deslocar de um lado para outro, no trabalho, nas actividades domésticas (femininas ou masculinas), na jardinagem e nas actividades que efectua no seu tempo livre para entretenimento, exercício ou desporto. As questões referem-se à actividade física que realiza numa ***semana normal*****,** e ***não em dias excepcionais*****,** como por exemplo, no dia em que fez a mudança da casa.

Por favor responda a todas as questões mesmo que não se considere uma pessoa activa.

Ao responder às seguintes questões considere o seguinte:
Actividade física vigorosa *refere-se* a *actividades que requerem muito esforço físico* e a *respiração fica muito mais intensa que o normal.*
Actividade física moderada *refere-se* a *actividades que requerem esforço físico moderado* e a *respiração fica* um *pouco mais intensa que o normal.*
Ao responder às questões considere apenas as *actividades físicas que realize durante pelo menos 10 minutos seguidos.*

1a Durante a última semana, quantos ***dias*** fez actividade física ***vigorosa*** como levantar e/ou transportar objectos pesados, cavar, realizar ginástica aeróbica, correr, nadar, jogar futebol ou andar de bicicleta a uma velocidade acelerada?
_________ dias por semana
_________ Nenhum (passe para a questão **2a**)
1b Quanto ***tempo***, no total, despendeu num desses dias, a realizar actividade física ***vigorosa***?
_________ horas _________ minutos

2a Durante a última semana, quantos ***dias*** fez actividade física ***moderada*** como levantar e/ou transportar objectos leves, andar de bicicleta a uma velocidade moderada, actividades domésticas (ex: esfregar, aspirar), cuidar do jardim, fazer trabalhos de carpintaria, jogar ténis de mesa? Não inclua o andar/caminhar.
__________ dias por semana
__________ Nenhum (passe para a questão **3a**)
2b Quanto ***tempo***, no total, despendeu num desses dias, a realizar actividade física moderada?
__________ horas _________ minutos

3a Durante a última semana, quantos dias ***andou/caminhou*** durante pelo menos 10 minutos seguidos? Inclua caminhadas para o trabalho e para casa, para se deslocar de um lado para outro e qualquer outra caminhada que possa fazer somente para recreação, desporto ou lazer.
___________ dias por semana
___________ Nenhum (passe para a questão **4a**)
3b Quanto ***tempo***, no total, despendeu num desses dias a andar/caminhar?
___________ horas ________ minutos
3c A que ***ritmo*** costuma caminhar?
_______**Vigoroso,** que toma a sua respiração muito mais intensa que o normal;
_______ **Moderado,** que toma a sua respiração um pouco mais intensa que o normal;
_______ **Lento,** que não causa qualquer alteração na sua respiração.

As últimas questões referem-se ao tempo que está sentado diariamente no trabalho, em casa, no percurso para o trabalho e durante os tempos livres. Estas questões incluem por exemplo **o tempo** *em que está* **sentado à mesa ou à secretária,** *a* **visitar amigos,** a **ler ou sentado/deitado** *a* **ver televisão.**

4a Quanto ***tempo***, no total, passou sentado(a) durante um dos dias de semana (segunda-feira a sexta-feira)?
_______ horas _______ minutos
4b Quanto ***tempo***, no total, passou sentado(a) durante um dos dias de fim-de-semana (sábado ou domingo)?
________ horas ________ minutos

Obrigado pela sua participação.

IPAQ-VERSÃOPORTUGUESA (CURTA) ** Adaptado de Mil-Homens, J (2004)*

Appendix 9: The Weight and Lifestyle Inventory (WALI).

Weight and Lifestyle Inventory, Wadden and Foster

The WALI is designed to obtain information about your weight and dieting histories, your eating and exercise habits, and your relationships with family and friends. Please complete the questionnaire carefully and make your best guess when unsure of the answer. Feel free to use the margins and bottom of pages when you need more space for your answers. You will have an opportunity to review your answers with a member of our professional staff.

Please allow 60-90 minutes to complete this questionnaire. Your answers will help us better identify problem areas and plan your treatment accordingly. Please be assured that the information you provide will be kept confidential and will only be available to the treatment staff. Thank you for taking the time to complete this questionnaire.

SECTION G: TOBACCO AND ALCOHOL USE

1. Do you currently smoke cigarettes? (Circle one.) Yes No
   If yes,
   a. How many do you smoke a day? _______
   b. How many years have you smoked? _______

2. Have you ever smoked cigarettes and stopped? (Circle one.) Yes No
   If yes,
   a. When did you stop smoking? _______
   b. How many cigarettes did you smoke? _______/day
   c. Did you experience any weight gain after stopping smoking? (Circle one.) Yes N
      If yes, how many pounds? _______

SECTION K: EATING PATTERNS II

Directions: Please circle ONE answer for each question.

1. How hungry are you usually in the morning?

0	1	2	3	4
Not at all	A little	Somewhat	Moderately	Very

2. When do you usually eat for the first time?

0	1	2	3	4
Before 9AM	9:01 to 12 PM	12:01 to 3PM	3:01 to 6PM	6:01 or later

3. Do you have cravings or urges to eat snacks after supper, but before bedtime?

0	1	2	3	4
Not at all	A little	Somewhat	Very much so	Extremely so

4. How much control do you have over your eating between supper and bedtime?

0	1	2	3	4
Not at all	A little	Some	Very much	Complete

5. How much of your daily food intake do you consume *after* suppertime?

0	1	2	3	4
0% (none)	1-25% (up to a quarter)	26-50% (about half)	51-75% (more than half)	76-100% (almost all)

6. Are you currently feeling blue or down in the dumps?

0	1	2	3	4
Not at all	A little	Somewhat	Very much so	Extremely

7. When you are feeling blue, is your mood lower in the:

0	1	2	3	4
Early Morning	Late Morning	Afternoon	Early Evening	Late Evening/Night

_____Check here if your mood does not change during the day.

8. How often do you have trouble getting to sleep?

0	1	2	3	4
Never	Sometimes	About half the time	Usually	Always

9. Other than only to use the bathroom, how often do you get up at least once in the middle of the night?

0	1	2	3	4
Never	Less than once a week	About once a week	More than once a week	Every night

**************** *IF 0 ON #9, PLEASE STOP HERE* ****************

10. Do you have cravings or urges to eat snacks when you wake up at night?

0	1	2	3	4
Not at all	A little	Somewhat	Very much so	Extremely so

11. Do you need to eat in order to get back to sleep when you awake at night?

0	1	2	3	4
Not at all	A little	Somewhat	Very much so	Extremely so

12. When you get up in the middle of the night, how often do you snack?

0	1	2	3	4
Never	Sometimes	About half the time	Usually	Always

**************** *IF 0 ON #12, PLEASE SKIP TO #15* ****************

13. When you snack in the middle of the night, how aware are you of your eating?

0	1	2	3	4
Not at all	A little	Somewhat	Very much so	Completely

14. How much control do you have over your eating while you are up at night?

0	1	2	3	4
None at all	A little	Some	Very much	Complete

15. How long have your difficulties with night eating been going on?

_____________ months _____________ years

The Night Eating Questionnaire is reprinted here from:
Allison KC, Stunkard AJ, Thier SL. Overcoming Night Eating Syndrome: A step-by-step guide to breaking the cycle. Oakland, CA: New Harbinger, 2004.

Weight and Lifestyle Inventory, Wadden and Foster

SECTION Q: MEDICAL HISTORY

1. Please indicate if you have had any of the medical conditions listed below:

	YES	NO
Heart Disease		
Angina (chest pains)		
Palpitations, heart beats fast or hard		
Stroke, mild stroke (cerebrovascular accident)		
Rheumatic fever		
Heart murmur		
Pacemaker		
Breathing problems (asthma, lung disease)		
High blood pressure		
Anemia		
Back problems		
Joint or bone problems		
Hiatal hernia		
Arthritis		
Gout (elevated uric acid)		
Gallbladder disease		
Thyroid problems		
Kidney disease		
Ulcers		
Bowel disease		
Liver disease		
Diabetes (type I or II)		
Sleep Apnea		
Bodily pain		
Other (specify)		

116S OBESITY Vol. 14 Supplement March 2006

Appendix 10: Patients' Global Impression of Change (PGIC)

Escala de Percepção Global de Mudança (PGIC versão Portuguesa)

Nome: ____ Data: ___________

Queixa principal: _________________________________

Desde o início do tratamento nesta instituição, como é que descreve a mudança (se houve) nas LIMITAÇÕES DE ACTIVIDADES, SINTOMAS, EMOÇÕES E QUALIDADE DE VIDA no seu global, em relação à sua dor (seleccione UMA opção):

Sem alterações (ou a condição piorou)	☐	1
Quase na mesma, sem qualquer alteração visível	☐	2
Ligeiramente melhor, mas, sem mudanças consideráveis	☐	3
Com algumas melhorias, mas a mudança não representou qualquer diferença real	☐	4
Moderadamente melhor, com mudança ligeira mas significativa	☐	5
Melhor, e com melhorias que fizeram uma diferença real e útil	☐	6
Muito melhor, e com uma melhoria considerável que fez toda a diferença	☐	7

Adaptado e Validado por: Domingues, L. & Cruz, E. (2011)

Appendix 11: Testimonials

"Olá Flávia, terminei este programa, (Pico) com grande alegria, não só por todas as pessoas que conheci, mas também pelos progressos alcançados. Cara Amiga Flávia, mais uma vez o meu muito Obrigado e fiquem certos de que vou ser o vosso Embaixador pelo mundo, publicitando o vosso Grandioso Trabalho, Abraços e beijinhos para todos,"

Sou Porfirio Brito, 07/2011

"Até à data está a funcionar em pleno.

Sinto-me mais solto de movimentos e... já perdi 3 Quilos!"

Joao Pinto

"Começámos o projecto PICO em meados de Março, no meu caso especifico já aconteceram algumas coisas boas: 1 - Comecei a sentir as minhas pernas mais fortes (joelhos) e estou a pouco e pouco a sentir que ando mais direita, com menos medo de por o pé esquerdo no chão, o que acontece normalmente.2- Descobri que o sofá lá de casa era muito baixo e que isso também me causava mais mal estar. Livrei-me do sofá, agora ou uso uma cadeira ou num sofá alto - tipo cama - em que não preciso de dobrar tanto as pernas.3 - Não sei se acontece a mais alguém, mas sinto mais dores no joelho quando parece que ele "sai do sitio" - descobri que se ficar de joelhos em cima duma almofada consigo "alinhar" essa parte do joelho e melhoro por uns tempos."

Um abraço para todos e obrigada por esta iniciativa !"

Maria Augusta Sousa 4 de Abril de 2011

"É com muito orgulho que faço parte desta grande equipa!

A Professora Flávia perguntou, eu pensei e aceitei. Uma porta abriu-se...para vos conhecer a todos!

Está a ser uma experiência incrível, ainda sou nova nestas andanças, estou a dar o meu melhor e espero vir a aprender com todos vocês. E espero que vocês, meus alunos e minhas alunas, aproveitem esta experiência para mudar as vossas vidas! grande sorriso

Não me posso esquecer da Joana, da Susana e do Kiko, que juntamente comigo, é a equipa que vos acompanhará até ao final e quiçá até mais uns meses.

Um Grande abraço a Todos! Obrigada! "

IOLA PINHO, 11/04/2011

" Olá a todos! Antes de tudo queria felicitar todos, mas todos os atletas que fazem parte desta jornada! Já tive a oportunidade de conhecer as 2 turmas (tarde e noite) e é fantástico ver a forma como vocês estão a aproveitar esta oportunidade! Isto é apenas o início. Daqui para a frente é só melhorar!! Toda a equipa está a trabalhar para isso!

Aproveito para agradecer à minha turma de "origem" (tarde) todas as alegrias que me têm proporcionado! É muito bom ouvir, com tão pouco tempo de aulas, que já sentem melhorias nas simples tarefas do dia-a-dia. Acreditem que só com o vosso esforço é que chegaram onde chegaram. Parabéns!

À turma da noite, que só tive, até então, a oportunidade de estar uma vez (mas que estarei mais vezes, com certeza) deixo um grande beijinho por serem tão simpáticos e nada de perderem a garra que eu vi quando vos dei aula, sim? grande sorriso Têm óptimos professores!

Saudações motricitárias,

Susana Valente - FMH (Projecto PICO)

"Como professor, só tenho que agradecer a determinação e empenho que demonstram aula após aula, pois os resultados não dependem só de quem vos acompanha fora de água, vocês são fundamentais em todo o processo. O vosso

desenvolvimento tem sido astronómico, basta pararem, pensarem, e olharem para o que faziam e o que estão neste momento a fazer, seja nas aulas ou no dia-a-dia. Para uns maiores, para outros mais pequenas, mas as diferenças são visíveis e no final, vão ter orgulho das horas que passaram na piscina a trabalhar, a suar, a queixarem-se que estavam cansado mas mesmo assim não desistiram, porque qualquer dificuldade ultrapassada é uma meta alcançada!!!

Como amigo, agradecer a oportunidade de vos ter conhecido! São fantásticos.

Como aluno, sinto-me na obrigação de agradecer pela terceira vez neste pequeno testemunho, pois num processo de aprendizagem contínua, esta é mais uma experiência em que estou a aprender e a evoluir como profissional da área do Exercício e Saúde, e vocês já fazem parte do meu desenvolvimento.

Todo o trabalho que está a ser desenvolvido tem passado por várias mãos e a competência e profissionalismo de quem lida com vocês, seja com maior, ou menor frequência, é uma mais valia para todo este processo. Obrigado a todos, sem exceção, que estão do lado de cá. O mérito do desenvolvimento dos alunos também é vosso!!!"

Um grande abraço,

Francisco Almeida Horta (Instrutor Hidroginástica - Projecto PICO)

PICO

Programa de Intervenção
Contra a Osteoartrose

Appendix 12: Yazigi F, Espanha M, Vieira F, Messier SP, Monteiro C, Veloso AP: The PICO project: aquatic exercise for knee osteoarthritis in overweight and obese individuals. BMC Musculoskelet Disord 2013, 14:320.

Yázigi et al. BMC Musculoskeletal Disorders 2013, 14:320
http://www.biomedcentral.com/1471-2474/14/320

BMC Musculoskeletal Disorders

STUDY PROTOCOL Open Access

The PICO project: aquatic exercise for knee osteoarthritis in overweight and obese individuals

Flávia Yázigi[1*], Margarida Espanha[1], Filomena Vieira[1], Stephen P Messier[2], Cristina Monteiro[1] and Antonio P Veloso[1]

Abstract

Background: Aquatic exercise is recommended by the Osteoarthritis Research Society (OARSI), by the American College of Rheumatology (ACR) and by the European League Against Rheumatism (EULAR) as a nonpharmacological method of controlling the knee osteoarthritis (KOA) symptoms. Moreover, given that weight loss results in a reduction of the load that is exerted upon the knee during daily activities, obesity is also considered to be a modifiable risk factor for the development and or exacerbation of KOA. The implementation of an exercise based weight loss program may, however, itself be limited by the symptoms of KOA. The aquatic program against osteoarthritis (termed "PICO" in Portuguese) prioritizes the control of symptoms and the recovery of functionality, with an attendant increase in the patient's physical activity level and, consequently, metabolic rate. Our laboratory is assessing the effectiveness of 3 months of PICO on the symptoms of KOA, on physical function, on quality of life and on gait. In addition, PICO shall examine the effects of said exercise intervention on inflammatory biomarkers, psychological health, life style and body composition.

Methods/Design: The trial is a prospective, single-blinded, randomized controlled trial, and involves 50 overweight and obese adults (BMI = 28–43.5 kg/m^2; age 40–65 yrs) with radiographic KOA. The participants are randomly allocated into either an educational attention (control) group or an aquatic (exercise program) group. This paper describes the experimental protocol that is used in the PICO project.

Discussion: The PICO program shall provide insight into the effectiveness of an aquatic exercise program in the control of KOA symptoms and in the improvement of the quality of life. As such, they are likely to prove a useful reference to health professionals who intend to implement any kind of therapeutic intervention based around aquatic exercise.

Trial registration: NCT01832545.

Keywords: Aquatic exercise, Knee osteoarthritis, Exercise, Pain, Obesity

Background

Although rheumatic diseases (RD) have low death rates, they are one of the primary causes of compromised quality of life and absenteeism from work, with attendant economic and social consequences [1]. In Portugal, RD are responsible for 40 to 60% of situations of prolonged physical incapacity in daily activities, for 43% of cases of absenteeism from work, and for 35 to 41% of early retirements due to illness [2].

Osteoarthritis (OA) is the most prevalent rheumatic disease and represents a great risk to the quality of life of the individual, given the consequent loss of autonomy that can be precipitated by its effect on lower extremity based activities (such as walking up and down stairs, climbing and squatting) [1,3,4]. Although the causes of OA are not completely understood, it is thought to be a complex, adaptive response of the joints to biomechanical, genetic and environmental stresses [5]. Recent studies demonstrated that that low-grade inflammation plays a pathophysiological role in OA. The severity, the symptoms, the impairment in physical function and the

* Correspondence: fyazigi@fmh.ulisboa.pt
[1]Department of Sports and Health, Univ de Lisboa, Fac Motricidade Humana, CIPER, LBMF, P-1499-002 Lisbon, Portugal
Full list of author information is available at the end of the article

progression of OA may also be partly mediated by the extent of chronic inflammation in OA patients [6,7].

The knee is the most commonly affected weight bearing joint, being considered the 4^{th} and 8^{th} main cause of disability in women and men, respectively [8]. KOA is more common in the medial tibiofemoral compartment than in other sites of the knee, probably due to a higher frequency of varus malalignment [9]. Inflammation and joint loading are commonly believed to cause or to exacerbate the disease process [10]. Obesity, prior knee injury, physical activity levels, physical strength and the extent of alignment/misalignment of body segments are the most often cited potential risk factors for KOA in the academic literature. The latter risk factor seems to have more importance in the radiographic progression than in the incidence of KOA [11-14].

Knee Osteoarthritis (KOA) is highly prevalent in obese individuals [15]. The International Association for the study of Obesity (IASO)/International Obesity Taskforce (IOTF) analysis (2010) estimated that approximately 1.0 billion adults are currently overweight and a further 475 million are obese, worldwide [16]. Obese individuals have higher concentrations of the inflammatory markers (such as TNF-α and leptin) that are predominantly secreted by adipose tissue and can induce the production of IL-6 and C-reactive protein (CRP) [17]. The pathogenesis of obesity is characterized by hypothalamic inflammation and subsequent central resistance to leptin. High leptin concentrations then compromise the reduction of food intake and increase in energy expenditure. In addition, leptin increases the synthesis of a stimulator of osteophyte formation, TNF-β [18]. The resulting low-grade inflammation plays a pathophysiological role in OA, because it can affect muscle function and lower the individual's pain threshold. It can also affect chondrocyte homeostasis and cause degenerative changes in cartilage [6,10,19].

Besides its effect on the individual's quality of life, KOA uses up considerable health care resources. The consequences of KOA make it a public health problem in many countries [1,20-22]. Pain is the symptom that markedly affects quality of life in KOA patients. Gait tests are an important measure of mobility and KOA patients may adapt their gait and adjust body alignment to reduce pain. However, the latter adaptations may increase the loading on the joint and result in increased disease progression. In addition, the pain that is concomitant with KOA causes irritability, sleeplessness, depression and other physical and psychological changes that may aggravate the disease and incur both a general loss of functionality and a drop or maintenance in physical activity levels to below the recommended levels [23]. The main consequences of inactivity are weight gain and the obesity installation [24]. The combination of obesity and KOA create a vicious cycle of pain, loss of functionality, and disease progression. To interrupt this cycle, KOA symptoms should be reduced. Physical activity and weight loss can make an important contribution.

Current therapy most often focuses on pain relief, using mainly analgesics and nonsteroidal anti-inflammatory medications that have only a modest functional benefit and do not slow disease progression, whilst causing serious cardiovascular and gastrointestinal side effects [25,26]. The recommendations of the Osteoarthritis Research Society International (OARSI), the American College of Rheumatology (ACR), and the European League Against Rheumatism (EULAR) also include exercise as an important treatment [27-29]. Aerobic, aquatic, and resistance training exercise are recommended [27].

Exercise program and Knee OA

Appropriate exercise can provide an improvement in symptoms and reduce pain, preventing OA-associated disabilities and increasing quality of life. In addition, there seems to be a positive effect of exercise on the chondroprotective anti-inflammatory cytokine response [30], mediated by IL-10 and IL-4. The weight loss and body composition improvements that can induced by exercise, reduce the thigh fat depots and may have a positive effect on the secretion of pro-inflammatory cytokines, lowering IL-1 and leptin levels in individuals with KOA [10].

The literature indicates that an exercise intervention for KOA should be broadly based and include aerobic training, lower limb-strengthening, gait training, flexibility, stability and posture training, weight reduction, patient education and psychosocial intervention [27,31-34].

Aquatic exercise is at this moment one of the main non pharmacological interventions that is suggested by the OARSI, ACR and EULAR guidelines as a means of controlling the symptoms and to prevent or slow down the progression of KOA [26,27,35]. Various studies have demonstrated that controlled aquatic exercise classes can be effective for KOA symptom control and to improve function [36-43]. In addition, a person in pain has difficulty with weight bearing exercise. Aquatic exercise allows aerobic exercise to be accomplished with less load on the joints [44].

Several studies have examined the effects of exercise in water (hydrotherapy, aquatic exercise) on the symptoms of knee arthritis [36-40,44-51]. However, said studies are inconsistent as regards the quality and quantity of exercise that was performed. There is a lack of definition of what is involved in hydrotherapy and what is performed in aquatic exercise classes. Aquatic Exercise (AE) is an exercise modality which can be defined as a group of exercises performed in the water, mainly in the vertical position, with or without music, with or without equipment added and in shallow or deep water. Its main characteristics are the utilisation of hydrostatic pressure and hydrodynamics to work on the aerobic and neuromuscular system. AE has been used for rehabilitation (hydrotherapy) [52-59], for athletic training [60-64] or for general fitness activity [65-71].

Aerobic training is very important for pain control and to improve functionality in individuals with KOA [27]. According to the guidelines of the Aquatic Exercise Association (AEA) [72], aerobic aquatic exercise classes with fitness goals, should be performed in water between 28-30°C so as not to compromising the endocrine responses. Water temperatures above 32°C are recommended for passive work, relaxation techniques or for individuals with low movement levels, but are not advisable temperature for aerobic or strength based exercise [64]. In cases of patients with low aquatic abilities, the Arthritis Foundation Guidelines suggest a superior limit range of water temperature of 31°C [73].

The PICO program is an overall body fitness and mind based intervention through aquatic exercise involving an educational component that has been specifically created for individuals with KOA. Two recent studies regarding the aquatic exercise in KOA should be referred to [38,39], as they have a controlled methodology and were performed according to the AEA guidelines [72].

Study aim

To design an aquatic exercise program specific to knee osteoarthritis, with the goal of management of OA symptoms and the improvement of physical fitness. The PICO program is based around the first step for weight loss interventions in individuals with KOA being the control of pain and other symptoms. When KOA symptoms are controlled, patients learn that it is possible to live with the disease which in turn motivates lifestyle changes. The increase of physical activity due to lifestyle changes may then cause improvement in body composition. In this way 6 hypotheses are formulated: H1. 3 months of aquatic exercise will improve KOA symptoms (pain and stiffness) and physical function in obese individuals with KOA; H2. The gait parameters (gait speed, gait cycle, ground reaction forces and knee forces moments) of obese individuals with KOA can be improved by aquatic exercise; H3. Beyond fitness component and the exercises skills, aquatic exercise group classes can work as an educational component and to promote lifestyle changes. H4: The aquatic exercise program can improve mental status and quality of life. H5: The aquatic exercise program can cause a weight reduction or body composition change. H6: 3 months of aquatic exercise can have a positive effect on selected inflammatory biomarkers of KOA.

Design/Methods

Study design

PICO is a single-blinded, randomized controlled trial with 3 months duration. Participants will be randomly assigned to one of two groups: aquatic exercise (AE) and control group (CG). Figure 1 provides a flowchart of PICO design. Researchers and personnel responsible for data collection will be blinded four the group classes. The study protocol was approved by the Ethical Committee of the Faculty of Human Kinetics, Technical University of Lisbon. All participants will be informed about the procedures and potential risks and an informed consent will be obtained from them.

Sample

Considering the calculation of the sample size, the studies of Messier (2009) [74] and Wang (2007) [44] were used as a reference, because they had a sample with similar characteristics and studied similar outcomes. Both showed that a reduction of symptoms in patients with OA of the knee led to a significant improvement ($\alpha < 0.05$) of the primary outcome measure of self-reported physical function. To find an analogous improvement of self-reported physical function of approximately 25% between the baseline and final measurements in patients with KOA, the minimum number of patients that are required is 20 for the main outcomes. The latter number is based on a power (1-B) of 0.80 and a significance level of 5% (two-sided). When a dropout rate of 20% is taken into account, at least 25 participants must be involved at study onset.

Inclusion criteria

The study sample will consist of 56 community-dwelling adults from the Lisbon area with: (1) age between 40 and 65 years; (2) $28.0 \leq \text{BMI} \leq 45$ kg/m^2; (3) unilateral or bilateral KOA diagnosed by knee pain and grade I-III radiographic tibiofemoral OA or tibiofemoral plus patellofemoral OA (4) a sedentary lifestyle, defined as not participating in a program that incorporates more than 30 minutes per week of formal exercise, within the 6 months leading up to the study; (5) being independently mobile; and (6) literate.

Exclusion criteria

The exclusion criteria are: subjects with skin diseases, with unstable medical conditions and or who have undergone hip or knee replacement, or knee surgery within the 6 months prior to the study; and participants who had any type of knee injections within the past 3 months.

Trial conduct

Recruitment

The recruitment and selection process will be done according to the aforesaid eligibility criteria. To avoid

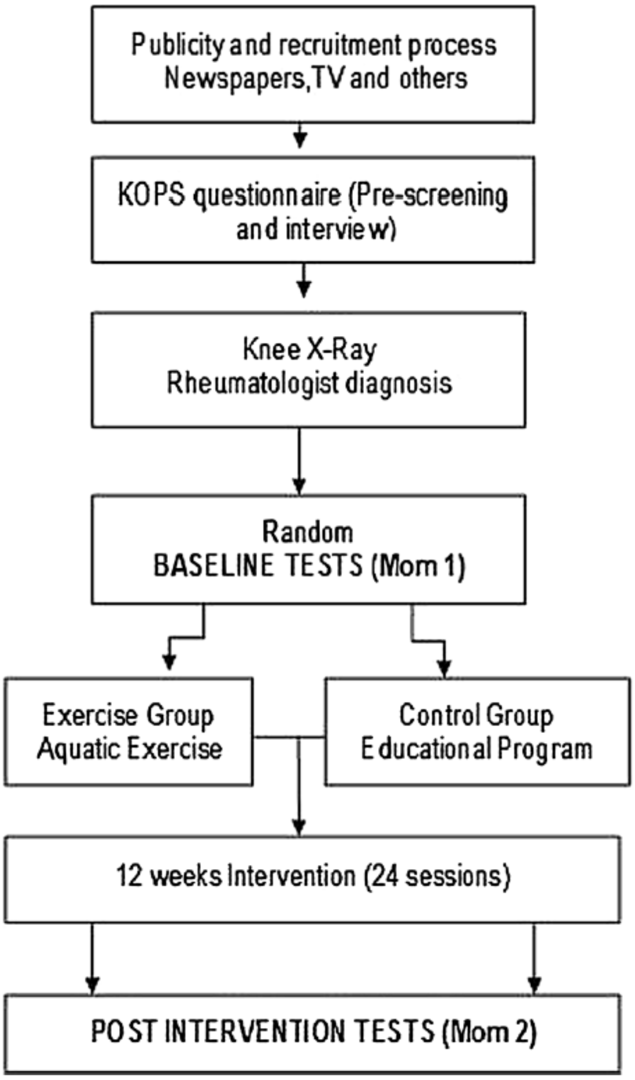


Figure 1 PICO flowchart.

convenience sampling different documents will be created for advertising and publicizing the PICO project. Social networks, television interviews, newspapers and the collaboration of entities/companies will be the main channels for PICO announcements.

All eligible individuals who contact the study secretariat will go through the same selection process, namely: a telephone based pre–selection stage followed by a face to face interview and completion of the screening questionnaire which will supply information about demographics and symptoms, signs and risk factors for KOA occurrence. Volunteers who, after completing the questionnaire, fulfill the ACR criteria for clinical diagnosis [75] will receive a request for an x-ray examination. The exams will be referred to a rheumatologist who will make the final diagnosis according to ACR radiological criteria. In the case of confirmation of the KOA diagnosis, the subject will be invited to a further interview the purpose of which is detailed explanation of the project, obtaining his/her informed consent and familiarization with both the locale and the equipment which shall be used in the tests.

Intervention programs

Aquatic exercise (AE)

The aquatic program is based on the guidelines of OARSI and EULAR for KOA management [28,29], on the Aquatic Exercise Association Guidelines (AEA) [72], on the Arthritis Foundation Aquatics Program instructor's manual [73], on the ACSM's Guidelines for Exercise Prescription [76] and on analysis of the protocols of previous studies [36,38,39,44,77,78].

The strategies in the PICO proposal to produce a high quality aquatic exercise intervention are structured according to AEA guidelines [72] and include overload assessment and managements, impact level control (level 1, 2 or 3), exercise cadence control and adequate music according to exercise goals. In addition the use of different and pre-defined cool-down sessions each week, a strong motivational component and pain assessment should make the difference in this protocol. Educational themes shall also be addressed during the classes. One educational theme per week shall be reinforced, such as: *What did you have for breakfast? Let's try, during this week, to improve the quality of our breakfast. Next class I will check what you ate; remember that you should assess yourself about knee pain, let's try to learn how to live with it.*

Another aspect that will be considered is the level of aquatic ability of each participant. Exercises like underwater breathing and flotation will be used in small doses to reduce fear of water and to ensure that participants are comfortable moving around the pool.

The aquatic program will be organized into 24 sessions distributed over 12 consecutive weeks, with a frequency of twice a week. The duration of each session will be 60 minutes, being that 10 minutes are for patient reception, blood pressure control, pain registry etc., and the effective time inside the water is 45 minutes. The indoor pool works with an air temperature around 27 ± 1°C and water temperature is controlled at 30.5 ± 0.5°C.

Table 1 describes the aquatic exercise class format for the first four weeks. Workouts are organized in order to have a progressive overload every week. Water is the main instrument to create resistance and only in the last week, according to the level of progression of the participants and whether their self-reported pain is controlled,

Table 1 The aquatic exercise protocol design for the first 4 weeks of the PICO program

Music BPM	Week1-5 (128 bpm)	Week 1	Week 2	Week 3	Week 4
Warm up (5-8′)	Duration	8′	8′	8′	8′
	Patterns	Walking combined with static and gentle movements of main joints. Use hands to keep thermal comfort	Walking combined with static and gentle movements of main joints	Walking combined with static and gentle movements of main joints	Walking combined with static and gentle movements of main joints
Aquatic adaptation		Vertical balance	Vertical balance	Submersion	Submersion
		Travellings	Travellings	Underwater breathing	Underwater breathing
Aerobic (15-30′)	Duration	3x5min	4x5′	4x5′	(1x10′) + 5′ + 5′
	Exercise pattern	Walking patterns with variation of upper limb patterns	Walking patterns with variation of upper limb patterns	Walking patterns with variation of upper limb patterns	10′ walking patterns + (2x5′) de basic aquatic patterns (Jumping jack, Ski, Leg Curl and Kicks)
	Intensity (%HRmax and RPE scale)	57%-67% RPE 4-6	57%-67% RPE 4-6	57%-67% RPE 4-6	64-74% RPE 5-6
Strength	Impact level	1	1	1	1
	Repetitions	2x8	1 x16	2x16	$2x16^{t1} + 1x8^{tt}$
	Cadence	t1 = water tempo	t1 = water tempo	t1 = water tempo	t1 = water tempo tt = land tempo
	Sets interval	Active 1-2′	Active 1-2′	Active 1-2′	Active 1-2′
	Equipment added	No	No	No	No
	Intensity (Omni-RES)	6-7	6-7	6-7	6-7
Cool down (5-6′)		Static stretching on the wall	Static stretching (center)	Dynamic/static stretching (center)	Dance + Dynamic/static

RPE- Rate of perceived exertion scale.

will additional equipment be added to increase the water resistance and consequently, the exercise overload. The Omni - Perceived Exertion Scale for Resistance Exercise (OMNI-RES) and for aerobic target zone (0–10 Borg Scale) will be used according guidelines for exercise intensity management [76].

The exercise instructors will use behavioral techniques: 1) to encourage social contact between participants; 2) to promote frequent contact during all intervention phases; 3) to define clear behavioral goals and allow feedback on achievements; 4) to help participants to self-monitor their pain and exercise intensity to complete activity; 5) to establish personal commitment to the project through the exercise leader.

Educational program: control group (CG)

The control group will not be enrolled in any exercise program but will participate in the educational program "PESO comunitário". This program is based on appropriate clinical guidelines and on validated behavior change principles [79]. Implemented by an intervention team with expertise gained from current scientific research in weight control determinants, this program, as is PICO, is free of charge for all interested adults who wish to manage their weight and health. It has operated since 2005 with the objective of preventing obesity or reducing excess weight as well as some of the risk factors for adult obesity, via through a change to steady healthy habits, attitudes and behaviors. PESO lasts 3 months and comprises 12 sessions of one and a half hour, on a weekly basis.

Measurements

Screening measurements

The Knee Osteoarthritis Pre-Screening questionnaire (KOPS) was validated by the authors and considered useful for this purpose (article in submission process). KOPS addresses physical function, activity level, co-morbid diseases, KOA risk factors and symptoms, height and weight (to determine BMI) as well as caregiver status. The demographic data that are collected include data on occupation, income, and educational level. The medical form is used to determine co-morbidities and to analyze any self-reported information on medications. The overall KOPS score has acceptable to good reliability with a Cronbach's Alpha of 0.747 and satisfactory internal consistency with an Intraclass Coefficient (ICC) for average measures of 0.646. The results for test-retest of one-week interval for each component ranged from 0.895-0.992 for ICC and from 0.894 to 0.979 for Cronbach's Alpha.

Osteoarthritis diagnosis and severity classification

To confirm OA and classify its severity the same X-ray protocol will be used for all subjects. Bilateral, anterior-posterior, weight-bearing knee radiographs will be used to identify OA in the tibiofemoral joint, and sunrise views to identify OA in the patellofemoral compartment. Severity of tibiofemoral OA will be measured using the K-L grading scale [80].

Outcomes, measures and instruments

All tests will be performed by all subjects at both baseline and 3 month later, at the end of the exercise intervention, using the same protocols and evaluated by the PICO team member(s). Tests list can be checked in the Table 2. The tests and questionnaires will be distributed over two nonconsecutive days, taking the fatigue levels of the subject and the need to avoid overload into account. Therefore the knee strength test and the Six Minute Walking Test will be conducted on different days.

The main outcomes will be KOA symptoms (pain and stiffness) and quality of life, physical function (aerobic

Table 2 Tests list

ASSESSMENT (TEST)	Screening	Baseline	3 months
Recruitment			
Interview	x		
KOPS	x		x
Knee X-ray (lateral and antero-posterior)	x		
KOA symptoms and quality of life (Self-reported questionnaires)			
Pain assessment (Brief pain inventory)		x	x
Knee osteoarthritis associated quality of life (KOOS)		x	x
MOS (SF-12v2)		x	x
Depression assessment (Beck depression inventory)		x	x
Weight and lifestyle inventory		x	x
Physical function and gait			
Aerobic capacity (6MWT)		x	x
Strength		x	x
Functional (FRSTS)		x	x
Knee (BIODEX dynamometer)		x	x
Hand (grip dynamometer)		x	x
Flexibility (CRS and BS tests)		x	x
Gait Analysis (Kinematics and kinetics)		x	x
Morphology and body composition			
Morphological measures (Anthropometry)		x	x
Body composition (DXA scan)		x	x
Life style			
Physical activity level (IPAQ)		x	x
Inflammation biomarkers			
Cytokines (blood drawn)		x	x

capacity, strength, and flexibility) and gait (kinetics and kinematics). The secondary outcomes are body composition, morphology, physical activity level, and inflammatory biomarkers. During the study, all participants will be allowed to maintain their usual medication, including analgesics and NSAIDs. A detailed record of medication will be done at baseline and 3 month post-intervention testing.

Knee OA symptoms and health quality of life

Brief Pain Inventory (BPI) – short version. A consensus panel, the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) recommended the inclusion of the short version of Brief Pain Inventory (BPI) in all trials that intend to assess chronic pain [81]. It is a widely used, reliable, valid instrument that assesses pain history, location, intensity and its interference with daily activities in individuals with osteoarthritis [82]. The Portuguese version was validated and recent studies have provided strong support for its reliability and validity [83,84].

Numerical Rating Scale (NRS). The subjects shall learn to self-assess their knee intensity pain via the 0–10 point NRS. The NRS should be used to control pain intensity before and after the aquatic exercise class and whenever is necessary.

Knee Injury and Osteoarthritis Outcome Score (KOOS). This questionnaire includes 5 dimensions to measure KOA specific health-related quality of life (QOL), knee pain (Pain), other disease-specific symptoms (Other Symptoms), activities of daily living (ADL), sport/recreation function (Sport/Rec). A score in each of the five dimensions is calculated as the sum of the items included and then converted according to a 0–100 scale, with 0 representing extreme knee problems and 100 representing no knee problems. The KOOS is validated for patients with knee injury or with knee OA and is a reliable and responsive self-administered instrument for short-termfollow-up [85]. The Portuguese validation has acceptable reliability with Cronbach's alpha coefficients between 0.77 and 0.95, and ICC ranging from 0.82 to 0.94 for the KOOS subscales [86].

Medical Outcomes Study **(MOS) Short-Form Health Survey (SF-12v2).** SF-12 v2 consists of a subset of 12 items to assess health status, organized into two domains: Physical (Physical Component Summary, PCS) and Psychological (Mental Component Summary, MCS) that make up the original SF-36 [87]. It has been shown that the SF-12 correlates highly with SF-36 in both obese and non-obese patients [88]. The Portuguese version of SF-12 has satisfactory reliability and validity [89,90].

Beck Depression Inventory (BDI-II). This instrument, developed by Beck and colleagues [91] has 21 items to rate the severity of depression according to the clinical definition. It is one of the most popular and widely used instruments for assessing the severity of depressive symptomatology. The Portuguese version [92] shows a good internal consistency, a factor structure very similar to the original version [91,93], and an adequate convergent validity.

Physical function

Six Minutes Walking Test (6MWT). The distance (d) and gait speed (v) of the 6MWT is used to assess the aerobic capacity and the walking ability. It will be performed individually and according to the *American Thoracic Society protocol* (ATS) [94], in a controlled indoor environment 46 meters in length and rectangular in shape. The 6MWT is highly reproducible in obese individuals ($r = 0.926$; 95% CI 0.816-0.972, $P < 0.001$) [95], and it has been used in studies with KOA [75,96-100].

Chair Sit and Reach test (CSR). The CSR test is a safe and socially acceptable alternative to traditional floor sit-and-reach tests as a reasonably accurate and stable measure of hamstring flexibility [101]. The subjects shall be allowed three attempts for each limb and the best of these scores shall be recorded to the nearest centimeter.

The Back Scratch Test (BS). The BSS is a measure of overall shoulder range of motion which involves measuring the distance between (or overlap of) the middle fingers behind the back with a ruler [102]. After a familiarization trial, this test is assessed twice, alternately with both hands, and the best value of each registered.

Five-Repetition Sit-To-Stand Test (FRSTST). This is a widely used measure of functional strength. ICC values for it demonstrate from good to high test-retest reliability for adults and subjects with osteoarthritis [100,103,104].

Strength

Knee Strength. A dynamometer Biodex System III (Biodex Medical Inc., Shirley, NY, U.S.A.) will be used for isokinetic assessment of knee strength (flexor and extensor muscles) and isometric knee strength, bilaterally. The first leg to be tested shall be the less affected leg or, in doubtful cases, the dominant leg. Gravity correction to torque is calculated at 45 degrees (0 = straight leg). The range of motion for testing is pre-determined from 20° to 80° for all subjects. The exclusion of extreme ranges of knee motion was established due to the fact that they are known to be painful and frequently non-executable by these patients, namely full extension due to quadriceps weakness Similar procedures, according to the dynamometer used, have been adopted in other surveys involving the same population [105-110].

Maximal Isokinetic Strength is measured on a concentric/concentric mode, at angular velocity of 60°/s. Among the low velocities' group, the 60°/s have been used in other studies and should provide better stability for this population [111]. The subjects should perform one set with minimum overload for habituation and 2 sets of 3 repetitions with a 120-second rest between sets. The subjects should be oriented to perform the test by exerting maximum pressure on the isokinetic arm through the entire range of movement. During the test vigorous verbal encouragement shall be given to each subject. The set with higher extension peak torque together with the lowest coefficient of variation will be chosen for analysis.

The angle of best torque of the knee extension obtained from each subject in the isokinetic test should be chosen for the isometric test. Maximal knee extension isometric test will be applied in one set of 3 repetitions during 5 seconds with 30 seconds relaxation interval between repetitions. The best of the three force-time curve will be chosen according to the higher peak.

Prior to measurement, the subject shall be are seated on the dynamometer with knee and hip joints at 90°. Crossover shoulder, belly and knee straps, as well as a lap belt will be used to restrain the subjects movement. The lever arm pad is strapped around the lower leg, 2 centimeters above the lateral malleolus of the fibula. The axis of rotation of the dynamometer should be aligned with knee joint's axis of rotation. Joint warm-up will be done by gentle free movements of flexion and extension of the knee.

The Handgrip Strength Test (HST). This test evaluates maximal isometric force of the muscles of the hand and forearm. Although the sample of this study will not have hand OA, this test has been used in obese individuals as an indicator of total body strength and functionality [112,113]. The adopted protocol for this project is the same that was used for Portuguese adults in the national observatory [114]. Prior to the test, the grip dynamometer should be adjusted to the size of the hand of each subject. Subject will be standing with arms along the body without contact with the trunk and elbow slightly bent at 200°. Testing is first done by dominant hand followed by the non-dominant one. The force must be performed during the expiratory phase and valsalva maneuver should be avoided. After three trials, if the difference between each value is within 3 kg, the test is considered completed. If a bigger difference is observed, then the test will be repeated after sufficient rest time. The best repetition will be chosen for further analysis.

Morphology and body composition

Body composition. Body mass index will be calculated as mass (measured in kilograms by a standard calibrated scale) divided by height squared (measured in meters). A DXA scanner (QDR 4500A, fan-beam densitometer, software version 8.21; Hologic, Waltham, USA) will be used to measure whole body lean mass (LM), fat mass (FM) and bone mineral content (BMC). DXA measures the attenuation of X-rays pulsed between 70 and 140 kV synchronously with the line frequency for each pixel of the scanned image. According to the protocol described by the manufacturer, a step phantom with six fields of acrylic and aluminum of varying thickness and known absorptive properties shall be scanned alongside each subject to serve as an external standard for the analysis of different tissue components. The same technician shall position the subjects, perform the scans and execute the analysis using the standard analysis protocol. Based on test-retest using 10 subjects, the coefficient of variation (CV) in PICO staff for FM and FFM was 2.6 and 1.5% respectively, and the total error of measurement (TEM) and the CV were 0.02 kg and 1.7% respectively.

Anthropometry. The anthropometric measurements that shall be collected by this study shall include height, body mass, perimeters (waist, hip, middle thigh, patella shank and foot breadth. The aforesaid measures shall be collected by an ISAK accredited anthropometrist using procedures established by ISAK [115] except in the case of patellar circumference, foot diameter and abdominal sagittal diameter, which shall be obtained according to previously validated procedures [116-118]. The intra-observer technical error for circumferences and diameters measures in the pilot study ranged from 0.2 -0.4.

Gait analysis

The gait protocol used on the present study was adapted from IDEA study [77], taking into account our laboratory specific equipment.

Data collection and analysis: Motion capture of the gait will be collected with 10 cameras Qualisys (Oqus-300) operating at a frame rate of 200Hz. Forty six reflective markers should be placed in predefined anatomical protuberances and used for the reconstruction of lower limb segments using Visual 3D software (C-Motion, Inc., Germantown, MD). To reduce noise, the motion data is filtered, using a low pass Butterworth filter, with a cutoff frequency of 15Hz [119]. Ground reaction force will be collected with two force platforms (Kistler AG, Winterthur, Switzerland) and AMTI (Advanced Mechanical Technology, Inc, Watertown, MA), synchronized with the motion capture system.

The test will be performed in a fifteen meters walkway, six successful trials are collected from each participant and three should be chosen for subsequent analysis. A trial consists of starting on the platform approximately 2 meters behind the initial timer and walking past the first beam of light to activate the timer. As the participant walks and passes the second beam of light the timer will stop and speed will be recorded. The participant will turn around and wait for orientations to perform similar trial in the opposite direction.

In general, KOA subjects walk at a slower speed and cadence, with a prolonged stance phase, presenting a static and dynamic varus alignment, showing smaller flexion and greater knee adduction moment (KAM) [12,34,120,121]. The following kinematic and kinetic outcomes should be analyzed from the gait test:

Gait speed
Freely chosen speed is slower in individuals with Knee OA being correlated with high ground reaction forces during heel strike [77];

Gait cycle characteristics
Swing and stance phase duration, stride frequency, stride length, knee and hip ROM and angular velocity;

Ground reaction forces
The vertical, anteroposterior and mediolateral force components will be recorded with a force platform. Computer software will be used to calculate duration, amplitude and impulse of the reaction forces;

Knee adduction moment (KAM)
Knee adduction moment (KAM) is considered a valid parameter to infer the level of mechanical loading [122]. Healthy subjects show substantially higher abduction moments than OA subjects and the external adductor moment has been linked to the development and progression of medial compartment OA in association with the varus alignment installation by increasing the compressive forces across the knee [123]. In addition, there is a significant inverse association between the peak of knee adduction moment during late stance and the amount of knee pain which may represent a compensatory mechanism to reduce medial tibiofemoral joint load in the setting of knee pain [124];

Adduction angular impulse (AddImp)
The integral of the frontal plane external joint moments (adduction and abduction) over time during the stance phase, providing a functional measure of gait rather than normalized KAM. This measure has been useful to distinguish loads in different OA severity [125,126];

Knee extension moment
Individuals with knee pain and weak muscles, as a protective mechanism, seem to avoid the quadriceps muscle recruitment during load acceptance in stance phase, showing a reduced knee peak extension moment;

Hip extensor moment
OA subjects walking at similar speeds of healthy one's maintain their walking speed by increasing hip range of motion and its speed. Greater hip extensor moments may indeed help to maintain walking speed, but this does not appear to be the case with the hip flexor and ankle plantar flexor moments, which were substantially lower;

Hip external abduction moment
Individuals with knee OA seems to have a higher involvement of hip adductor muscles to compensate a weak quadriceps and hip abductors [12,127].

Since this is a longitudinal study, walking speed may change and should be measured at each testing moment (baseline and after intervention). One successful trial is defined as the one in which the participant's entire foot is placed on the surface area of the force platform while walking within ± 3.5% of the freely chosen speed.

The freely chosen speed should be assessed in the biomechanical test day before the placement of markers, in so far as each subject shall walk barefoot in the walkway until a stabilization of walking speed is observed. Usually the latter stabilization occurs after crossing of the walkway 5–6 times. The speed is monitored using an infrared photocell control system (Model E3F2-R4B4-M, OMRON) set with 7.3 m apart at the hip level, interfaced with a processor specifically built to record the time and calculate the speed as a function of the distance.

Lifestyle
International physical activity questionnaire (IPAQ)
The short form of IPAQ was chosen because it is easy to apply. Despite its liability having been verified in many countries and with different populations [128-130], studies have indicated that the IPAQ-SF typically overestimates physical activity [131]. However, this instrument will be used for controlling the amount of physical activity along the study, and not for any classification of physical activity level. All participants shall receive a previous explanation about how to complete the questionnaire, and their

answers will be confirmed during the interview. Data will be processed according to IPAQ guidelines [132].

The weight and lifestyle inventory (WALI)

The WALI is designed to obtain demographics information, weight and dieting histories, eating and exercise habits, and relationships with family and friends [133]. The Portuguese version (IPEV) and the process by which it was translated is published in a national book [134]. The PICO project will use only the sections G, K and Q of the Portuguese version (IPEV) for controlling alcohol and tobacco consumption, dietary patterns and clinical historic.

Inflammatory biomarkers

Our primary measures are IL-6 and IL-10. These cytokines are consistently implicated in OA pathogenesis and showed significant improvement with weight loss in ADAPT. We will also measure hsCRP as an overall marker of chronic inflammation and TNFα and TNFα soluble receptor 1 (sTNFR1) because they are also implicated in OA pathogenesis. Leptin, an adipokine that increases synthesis of TGFβ, a known stimulator of osteophyte formation, will also be measured.

For assessing IL-6, IL-10, hsCRP, TNFα, sTNFαR1 and leptin, venous blood samples (approximately 10 ml per visit) will be collected into dry tubes and EDTA tubes by standard procedures in the morning after a minimum of 4 h fast without any type of exercise.

Blood will be centrifuged at 1500 x g for 10 min to separate serum from the cloth in the dry tubes and plasma from red blood cells in the EDTA tubes. Serum and plasma will be frozen at 80°C for posterior analysis by ELISA using commercially available kits.

Statistical analysis

Descriptive statistics, including frequencies for categorical variables and means with standard deviations (SD) for continuous variables with normal distribution and median for skewed distributions will be used to describe subject's characteristics. Normality will be tested using the Kolmogorov-Smirnov test. For continuous outcome measures, differences in mean change (baseline minus post-intervention) will be compared between groups using analysis of covariance adjusted for baseline values of the outcome. Comparisons between groups (CG and AEG) at baseline and post intervention will be conducted by Independent-sample t-tests or Mann–Whitney U test if equal variance is not assumed. Changes within group will be analyzed by paired Student's t tests or by the Wilcoxon Signed Rank test when normality is not assumed. A mixed model analyses of covariance (ANCOVAs) will be conducted for interaction analyses adjusted for BMI with two within-participant factors of 6MWT (baseline) and 6MWT (post-intervention) and between two groups (CG and AE). Statistical analysis will be performed using IBM SPSS Statistics 20.0 and MedCalc Statistical Software (MedCalc Software, Mariakerke, Belgium). Multiple Linear regression analyses will be performed to understand the potential covariates that could improve the explanation of the variability of outcomes (6MWT, strength and KOOS dimensions). Statistical significance will be set at $P < 0.05$ (2- tailed) for all analyses. Effect sizes will be calculated for all measures with an effect size of 0.2 considered small, 0.5 medium and 0.8 large.

Discussion

The need to improve non-pharmacological intervention for patients with KOA is obvious, and aquatic exercise is an option for obese patients since it minimizes joint load. Although water exercise is frequently encouraged, relatively little research has been conducted in this area as compared to land-based exercise.

There are several strengths to the design of this study. The first one, is the detailed exercise prescription protocol concerning dosage (frequency, duration and intensity of the exercise), the fulfillment of overload and individuality principles of training (e.g., gradual increase of the number of sets and repetitions on strength training), and the control of exercise intensity during the sessions using rating perception effort scales (e.g., Borg RPE and Omni scales).

Secondly, the pool where the program will be delivered is easily accessed by train or bus. This aspect is crucial as the access to appropriate facilities and patient motivation to undertake water exercise, might be a barrier to adherence. Additionally, the fact of our sample being adult and not elderly should facilitate the displacement to our facilities.

Thirdly, the exercise program will be delivered by high qualified aquatic exercise instructors, all of whom shall be graduates in Sports Science at the Faculty of Human Kinetics who have specialized in exercise and health and fitness group skills. The exercise program will be delivered similarly to both classes regarding exercises, overloads and leading strategies according to the predefined plan. Four instructors will be organized in pairs, and each pair will take care of one aquatic exercise group during the entire program.

With the exception of the knee radiographs for OA diagnosis, all measures will be obtained in the same facility at the baseline and immediately after the end of the program. One barrier at each visit/measuring point will be the capacity to asses all participants in a short interval. Due to the specificity of the outcomes will be necessary to manage the schedule among four different labs. Therefore, to support the project, staff team includes one secretary responsible for administrative work, four technicians conducting the dynamometer tests, gait analysis, body composition and anthropometry assessments and one professional for collecting blood samples. Each technician received the responsibility to be specialized in two test's group plus questionnaires and, to avoid inter-rater error, the same technician should lead its application in both assessments, baseline and post-exercise intervention. Participant adherence to exercise is one of the main challenges, therefore to avoid drop outs, motivational cues, intra-group social interaction, frequent telephone calls and the quality of instructors are the main strategies chosen to contribute to adherence rates. Besides, since our sample will include adults that may still be working which will create some difficulties in the definition of class schedules, one extra class, every 15 days, will be provided to enhance high compliance, and to allow that all participants might attend to 24 sessions during the 3 month period over which the study shall run.

One possible constraint to the success of the aquatic exercise programs would be the level of water skills of each participant. Although it is not necessary to know how to swim, the autonomy and the ability to apply power against the water are essential to get benefits from this type of activity, especially when performing strengthening exercises. Therefore some aquatic adaptation exercises will be introduced in the class format (Table 1).

Our study is based on the premise that individuals with KOA need a wide exercise intervention, adapted not only to the affected joint but to the health status of the patient, working the whole body and the mind simultaneously. In addition, we expect that aquatic exercise, beyond the improvement of KOA symptoms, can increase the symmetry between forces in the lower-limb joints (adduction/abduction and flexion/extension moments at knee and hip joints), so improving gait.

The format of the sessions, the study duration and the weekly frequency of exercise classes are organized in such a way as to make sure that this proposal is executable, not only for this project but also for future implementations by communities or in private pools. The sample size of this protocol are reduced because we consider that, before implementing the program in the general community, for public health, the exercise protocol should be validated by a very controlled process.

Conclusions

This study is a Randomized Controlled Trial (RCT) using aquatic exercise specially designed with a very controlled methodology. It is expected that the results will enable evidence-based recommendations for the treatment of patients with KOA through aquatic-exercise. Future studies would aim to reproduce the protocol contained herein and implement it in a larger sample and in different communities. The findings of PICO's aquatic program for KOA should inform the development of an effective and reproducible exercise protocol, available for use by any professional with aquatic exercise and exercise and health related knowledge.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

FY conceived the study, participated in its design and coordination, shall carry out the biomechanical gait tests, the intervention team coordination and drafted the manuscript. ME participated in its design, coordinates staff, and improved both the manuscript improvement and data management. SM participated in the protocol development, and in training staff for biomechanics tests. FV participated in the design of the body composition and anthropometry based protocols and their coordination. CM coordinates and carries out the biomarker analyses. AV participated in the study design and manuscript improvement. All authors read and made comments on previous drafts of the manuscript, and approved the final manuscript.

Acknowledgements

We gratefully acknowledge the contributions to this paper of our colleagues and also, a special thanks to Professor Veronica Vleck for the final revision.

Author details

[1]Department of Sports and Health, Univ de Lisboa, Fac Motricidade Humana, CIPER, LBMF, P-1499-002 Lisbon, Portugal. [2]Department of Health and Exercise Science, Wake Forest University, Winston-Salem, NC, USA.

Received: 29 May 2013 Accepted: 7 November 2013
Published: 13 November 2013

References

1. Arden N, Nevitt MC: **Osteoarthritis: epidemiology.** *Best Pract Res Clin Rheumatol* 2006, **20**:3–25.
2. DGS: *Programa nacional contra as doenças reumáticas: circular normativa, Saúde DGd ed., vol. 12 DGCG edition.* Portugal: DGS; 2004.
3. Gabriel SE, Michaud K: **Epidemiological studies in incidence, prevalence, mortality, and comorbidity of the rheumatic diseases.** *Arthritis Res Ther* 2009, **11**:229.
4. Issa SN, Sharma L: **Epidemiology of osteoarthritis: an update.** *Curr Rheumatol Rep* 2006, **8**:7–15.
5. Dieppe P: *Osteoarthritis. Acta Orthop Scand Suppl* 1998, **281**:2–5.
6. van der Kraan PM: **Osteoarthritis year 2012 in review: biology.** *Osteoarthritis Cartilage* 2012, **20**:1447–1450.
7. Rai MF, Sandell LJ: **Inflammatory mediators: tracing links between obesity and osteoarthritis.** *Crit Rev Eukaryot Gene Expr* 2011, **21**:131–142.
8. Williams F, Spector T: *Osteoarthritis. Medicine* 2006, **34**:364–368.
9. Winby CR, Lloyd DG, Besier TF, Kirk TB: **Muscle and external load contribution to knee joint contact loads during normal gait.** *J Biomech* 2009, **42**:2294–2300.
10. Messier SP: **Obesity and osteoarthritis: disease genesis and nonpharmacologic weight management.** *Rheum Dis Clin North Am* 2008, **34**:713–729.
11. Cerejo R, Dunlop DD, Cahue S, Channin D, Song J, Sharma L: **The influence of alignment on risk of knee osteoarthritis progression according to baseline stage of disease.** *Arthritis Rheum* 2002, **46**:2632–2636.
12. Chang A, Hayes K, Dunlop D, Song J, Hurwitz D, Cahue S, Sharma L: **Hip abduction moment and protection against medial tibiofemoral osteoarthritis progression.** *Arthritis Rheum* 2005, **52**:3515–3519.
13. Cooper C, Snow S, McAlindon TE, Kellingray S, Stuart B, Coggon D, Dieppe PA: **Risk factors for the incidence and progression of radiographic knee osteoarthritis.** *Arthritis Rheum* 2000, **43**:995–1000.
14. Hunter DJ, Sharma L, Skaife T: **Alignment and osteoarthritis of the knee.** *J Bone Joint Surg Am* 2009, **91**(1):85–89.
15. Martin KR, Kuh D, Harris TB, Guralnik JM, Coggon D, Wills AK: **Body mass index, occupational activity, and leisure-time physical activity: an exploration of risk factors and modifiers for knee osteoarthritis in the 1946 British birth cohort.** *BMC Musculoskelet Disord* 2013, **14**:219.

16. *The global epidemic: IASO/IOTF analysis.* http://www.iaso.org/iotf/obesity/obesitytheglobalepidemic/.
17. Bullo M, Garcia-Lorda P, Megias I, Salas-Salvado J: **Systemic inflammation, adipose tissue tumor necrosis factor, and leptin expression.** *Obes Res* 2003, **11:**525–531.
18. Scharstuhl A, Glansbeek HL, van Beuningen HM, Vitters EL, van der Kraan PM, van den Berg WB: **Inhibition of endogenous TGF-beta during experimental osteoarthritis prevents osteophyte formation and impairs cartilage repair.** *J Immunol* 2002, **169:**507–514.
19. Mobasheri A: **Osteoarthritis year 2012 in review: biomarkers.** *Osteoarthritis Cartilage* 2012, **20:**1451–1464.
20. Bitton R: **The economic burden of osteoarthritis.** *Am J Manag Care* 2009, **15:**S230–235.
21. Zhang Y, Jordan JM: **Epidemiology of osteoarthritis.** *Clin Geriatr Med* 2010, **26:**355–369.
22. Jordan JM, Helmick CG, Renner JB, Luta G, Dragomir AD, Woodard J, Fang F, Schwartz TA, Abbate LM, Callahan LF, *et al*: **Prevalence of knee symptoms and radiographic and symptomatic knee osteoarthritis in African Americans and Caucasians: the Johnston county osteoarthritis project.** *J Rheumatol* 2007, **34:**172–180.
23. Farr JN, Going SB, Lohman TG, Rankin L, Kasle S, Cornett M, Cussler E: **Physical activity levels in patients with early knee osteoarthritis measured by accelerometry.** *Arthritis Rheum* 2008, **59:**1229–1236.
24. Flegal KM, Carroll MD, Ogden CL, Johnson CL: **Prevalence and trends in obesity among US adults, 1999–2000.** *JAMA* 2002, **288:**1723–1727.
25. Richmond J, Hunter D, Irrgang J, Jones MH, Levy B, Marx R, Snyder-Mackler L, Watters WC 3rd, Haralson RH 3rd, Turkelson CM, *et al*: **Treatment of osteoarthritis of the knee (nonarthroplasty).** *J Am Acad Orthop Surg* 2009, **17:**591–600.
26. Zhang W, Moskowitz RW, Nuki G, Abramson S, Altman RD, Arden N, Bierma-Zeinstra S, Brandt KD, Croft P, Doherty M, *et al*: **OARSI recommendations for the management of hip and knee osteoarthritis, part II: OARSI evidence-based, expert consensus guidelines.** *Osteoarthritis Cartilage* 2008, **16:**137–162.
27. Hochberg MC, Altman RD, April KT, Benkhalti M, Guyatt G, McGowan J, Towheed T, Welch V, Wells G, Tugwell P: **American college of rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee.** *Arthritis Care Res (Hoboken)* 2012, **64:**465–474.
28. Jordan KM, Arden NK, Doherty M, Bannwarth B, Bijlsma JW, Dieppe P, Gunther K, Hauselmann H, Herrero-Beaumont G, Kaklamanis P, *et al*: **EULAR recommendations 2003: an evidence based approach to the management of knee osteoarthritis: report of a task force of the standing committee for international clinical studies including therapeutic trials (ESCISIT).** *Ann Rheum Dis* 2003, **62:**1145–1155.
29. Zhang W, Nuki G, Moskowitz RW, Abramson S, Altman RD, Arden NK, Bierma-Zeinstra S, Brandt KD, Croft P, Doherty M, *et al*: **OARSI recommendations for the management of hip and knee osteoarthritis: part III: changes in evidence following systematic cumulative update of research published through january 2009.** *Osteoarthritis Cartilage* 2010, **18:**476–499.
30. Helmark IC, Mikkelsen UR, Borglum J, Rothe A, Petersen MC, Andersen O, Langberg H, Kjaer M: **Exercise increases interleukin-10 levels both intraarticularly and peri-synovially in patients with knee osteoarthritis: a randomized controlled trial.** *Arthritis Res Ther* 2010, **12:**R126.
31. Bennell KL, Hinman RS: **A review of the clinical evidence for exercise in osteoarthritis of the hip and knee.** *J Sci Med Sport* 2011, **14:**4–9.
32. Bosomworth NJ: **Exercise and knee osteoarthritis: benefit or hazard?** *Can Fam Physician* 2009, **55:**871–878.
33. Roddy E, Zhang W, Doherty M, Arden NK, Barlow J, Birrell F, Carr A, Chakravarty K, Dickson J, Hay E, *et al*: **Evidence-based recommendations for the role of exercise in the management of osteoarthritis of the hip or knee–the MOVE consensus.** *Rheumatology (Oxford)* 2005, **44:**67–73.
34. Mundermann A, Dyrby CO, Hurwitz DE, Sharma L, Andriacchi TP: **Potential strategies to reduce medial compartment loading in patients with knee osteoarthritis of varying severity: reduced walking speed.** *Arthritis Rheum* 2004, **50:**1172–1178.
35. Zhang W, Moskowitz RW, Nuki G, Abramson S, Altman RD, Arden N, Bierma-Zeinstra S, Brandt KD, Croft P, Doherty M, *et al*: **OARSI recommendations for the management of hip and knee osteoarthritis, part I: critical appraisal of existing treatment guidelines and systematic review of current research evidence.** *Osteoarthritis Cartilage* 2007, **15:**981–1000.
36. Bartels EM, Lund H, Hagen KB, Dagfinrud H, Christensen R, Danneskiold-Samsoe B: **Aquatic exercise for the treatment of knee and hip osteoarthritis.** *Cochrane Database Syst Rev* 2007, **17**(4):CD005523.
37. Hinman RS, Heywood SE, Day AR: **Aquatic physical therapy for hip and knee osteoarthritis: results of a single-blind randomized controlled trial.** *Phys Ther* 2007, **87:**32–43.
38. Lim JY, Tchai E, Jang SN: **Effectiveness of aquatic exercise for obese patients with knee osteoarthritis: a randomized controlled trial.** *PM R* 2010, **2:**723–731. quiz 793.
39. Wang TJ, Lee SC, Liang SY, Tung HH, Wu SF, Lin YP: **Comparing the efficacy of aquatic exercises and land-based exercises for patients with knee osteoarthritis.** *J Clin Nurs* 2011, **20:**2609–2622.
40. Wyatt FB, Milam S, Manske RC, Deere R: **The effects of aquatic and traditional exercise programs on persons with knee osteoarthritis.** *J Strength Cond Res* 2001, **15:**337–340.
41. Tsourlou T, Benik A, Dipla K, Zafeiridis A, Kellis S: **The effects of a twenty-four-week aquatic training program on muscular strength performance in healthy elderly women.** *J Strength Cond Res* 2006, **20:**811–818.
42. Driver S, O'Connor J, Lox C, Rees K: **Evaluation of an aquatics programme on fitness parameters of individuals with a brain injury.** *Brain Inj* 2004, **18:**847–859.
43. Templeton MS, Booth DL, O'Kelly WD: **Effects of aquatic therapy on joint flexibility and functional ability in subjects with rheumatic disease.** *J Orthop Sports Phys Ther* 1996, **23:**376–381.
44. Wang TJ, Belza B, Elaine Thompson F, Whitney JD, Bennett K: **Effects of aquatic exercise on flexibility, strength and aerobic fitness in adults with osteoarthritis of the hip or knee.** *J Adv Nurs* 2007, **57:**141–152.
45. Liebs TR, Herzberg W, Ruther W, Haasters J, Russlies M, Hassenpflug J: **Multicenter randomized controlled trial comparing early versus late aquatic therapy after total hip or knee arthroplasty.** *Arch Phys Med Rehabil* 2012, **93:**192–199.
46. Valtonen A, Poyhonen T, Sipila S, Heinonen A: **Maintenance of aquatic training-induced benefits on mobility and lower-extremity muscles among persons with unilateral knee replacement.** *Arch Phys Med Rehabil* 2011, **92:**1944–1950.
47. Escalante Y, Saavedra JM, Garcia-Hermoso A, Silva AJ, Barbosa TM: **Physical exercise and reduction of pain in adults with lower limb osteoarthritis: a systematic review.** *J Back Musculoskelet Rehabil* 2010, **23:**175–186.
48. Rahmann AE, Brauer SG, Nitz JC: **A specific inpatient aquatic physiotherapy program improves strength after total hip or knee replacement surgery: a randomized controlled trial.** *Arch Phys Med Rehabil* 2009, **90:**745–755.
49. Lee HY: **Comparison of effects among Tai-Chi exercise, aquatic exercise, and a self-help program for patients with knee osteoarthritis.** *Taehan Kanho Hakhoe Chi* 2006, **36:**571–580.
50. **Aquatic physical therapy: running in water decreases stress on the body.** *J Orthop Sports Phys Ther* 2012, **42:**445.
51. Verhagen AP, Cardoso JR, Bierma-Zeinstra SM: **Aquatic exercise & balneotherapy in musculoskeletal conditions.** *Best Pract Res Clin Rheumatol* 2012, **26:**335–343.
52. Ariyoshi M, Sonoda K, Nagata K, Mashima T, Zenmyo M, Paku C, Takamiya Y, Yoshimatsu H, Hirai Y, Yasunaga H, *et al*: **Efficacy of aquatic exercises for patients with low-back pain.** *Kurume Med J* 1999, **46:**91–96.
53. Bacon MC, Nicholson C, Binder H, White PH: **Juvenile rheumatoid arthritis: aquatic exercise and lower-extremity function.** *Arthritis Care Res* 1991, **4:**102–105.
54. Hall J, Grant J, Blake D, Taylor G, Garbutt G: **Cardiorespiratory responses to aquatic treadmill walking in patients with rheumatoid arthritis.** *Physiother Res Int* 2004, **9:**59–73.
55. Kelly M, Darrah J: **Aquatic exercise for children with cerebral palsy.** *Dev Med Child Neurol* 2005, **47:**838–842.
56. Kargarfard M, Dehghadani M, Ghias R: **The effect of aquatic exercise therapy on muscle strength and Joint's range of motion in hemophilia patients.** *Int J Prev Med* 2013, **4:**50–56.
57. Kallberg J: **Aquatic therapy brings relief: arthritis sufferers go back to the future to achieve freedom from pain, courtesy of technological advances in an old remedy.** *Provider* 2013, **39:**35–37.
58. Cantarero-Villanueva I, Fernandez-Lao C, Cuesta-Vargas AI, Del Moral-Avila R, Fernandez-de-Las-Penas CC, Arroyo-Morales M: **The effectiveness of a deep water aquatic exercise program in cancer-related fatigue in breast**

cancer survivors: a randomized clinical trial deep water aquatic exercise in cancer survivors. *Arch Phys Med Rehabil* 2012, **94**(2):221–230.
59. Barakat R, Cordero Y, Coteron J, Luaces M, Montejo R: **Exercise during pregnancy improves maternal glucose screen at 24–28 weeks: a randomised controlled trial.** *Br J Sports Med* 2012, **46**:656–661.
60. DeMaere JM, Ruby BC: **Effects of deep water and treadmill running on oxygen uptake and energy expenditure in seasonally trained cross country runners.** *J Sports Med Phys Fitness* 1997, **37**:175–181.
61. Martel GF, Harmer ML, Logan JM, Parker CB: **Aquatic plyometric training increases vertical jump in female volleyball players.** *Med Sci Sports Exerc* 2005, **37**:1814–1819.
62. Reilly T, Ekblom B: **The use of recovery methods post-exercise.** *J Sports Sci* 2005, **23**:619–627.
63. Alberton CL, Cadore EL, Pinto SS, Tartaruga MP, da Silva EM, Kruel LF: **Cardiorespiratory, neuromuscular and kinematic responses to stationary running performed in water and on dry land.** *Eur J Appl Physiol* 2011, **111**:1157–1166.
64. Yazigi F, Pinto S, Colado J, Escalante Y, Armada-Da-Silva P, Brasil R, Alves F: **The cadence and water temperature effect on physiological responses during water cycling.** *European Journal of Sport Science* 2013:1–7.
65. Water exercise for arthritis: **Low-impact fitness.** *Mayo Clin Health Lett* 2003, **21**:4–5.
66. Broman G, Quintana M, Engardt M, Gullstrand L, Jansson E, Kaijser L: **Older women's cardiovascular responses to deep-water running.** *J Aging Phys Act* 2006, **14**:29–40.
67. Brown SP, Chitwood LF, Beason KR, McLemore DR: **Physiological correlates with perceived exertion during deep water running.** *Percept Mot Skills* 1996, **83**:155–162.
68. Butts NK, Tucker M, Greening C: **Physiologic responses to maximal treadmill and deep water running in men and women.** *Am J Sports Med* 1991, **19**:612–614.
69. Chu KS, Rhodes EC: **Physiological and cardiovascular changes associated with deep water running in the young. Possible implications for the elderly.** *Sports Med* 2001, **31**:33–46.
70. Triplett NT, Colado JC, Benavent J, Alakhdar Y, Madera J, Gonzalez LM, Tella V: **Concentric and impact forces of single-leg jumps in an aquatic environment versus on land.** *Med Sci Sports Exerc* 2009, **41**:1790–1796.
71. Phillips VK, Legge M, Jones LM: **Maximal physiological responses between aquatic and land exercise in overweight women.** *Med Sci Sports Exerc* 2008, **40**:959–964.
72. Aquatic Exercise Association: *Aquatic fitness professional manual 5 edn.* Nokomis, FL; 2006.
73. Foundation A: *Arthritis foundation YMCA aquatic program (AFYAP) and AFYAP PLUS instructor's guides 4th edn.* The Arthritis Foundation: Atlanta; 2002.
74. Messier SP: **Obesity and osteoarthritis: disease genesis and nonpharmacologic weight management.** *Med Clin North Am* 2009, **93**:145–159. xi-xii.
75. Altman R, Alarcon G, Appelrouth D, Bloch D, Borenstein D, Brandt K, Brown C, Cooke TD, Daniel W, Feldman D, *et al*: **The American college of rheumatology criteria for the classification and reporting of osteoarthritis of the hip.** *Arthritis Rheum* 1991, **34**:505–514.
76. American College of Sports Medicine (ACSM): *ACSM's guidelines for exercise testing and prescription.* 8th edition. Lippincott Williams & Wilkins; 2009.
77. Messier SP, Legault C, Mihalko S, Miller GD, Loeser RF, DeVita P, Lyles M, Eckstein F, Hunter DJ, Williamson JD, Nicklas BJ: **The intensive diet and exercise for arthritis (IDEA) trial: design and rationale.** *BMC Musculoskelet Disord* 2009, **10**:93.
78. Batterham SI, Heywood S, Keating JL: **Systematic review and meta-analysis comparing land and aquatic exercise for people with hip or knee arthritis on function, mobility and other health outcomes.** *BMC Musculoskelet Disord* 2011, **12**:123.
79. Silva M, Santos T, Coutinho S, Marcelino M, Vieira P, Tomás R, Carraça E, Minderico C, Sardinha L, Teixeira P: **O programa "PESO COMUNITÁRIO.** *Revista de Informação e Divulgação Científica sobre Doenças do Comportamento Alimentar* 2008, **5**:1–12.
80. Kellgren JH, Lawrence JS: **Radiological assessment of osteo-arthrosis.** *Ann Rheum Dis* 1957, **16**:494–502.
81. Turk DC, Dworkin RH, Allen RR, Bellamy N, Brandenburg N, Carr DB, Cleeland C, Dionne R, Farrar JT, Galer BS, *et al*: **Core outcome domains for chronic pain clinical trials: IMMPACT recommendations.** *Pain* 2003, **106**:337–345.
82. Mendoza T, Mayne T, Rublee D, Cleeland C: **Reliability and validity of a modified brief pain inventory short form in patients with osteoarthritis.** *Eur J Pain* 2006, **10**:353–361.
83. Ferreira-Valente MA, Pais Ribeiro JL, Jensen MP: **Further validation of a Portuguese version of the brief pain inventory interference scale.** *Clínica y Salud* 2012, **23**:89–96.
84. Azevedo LF, Pereira AC, Dias C, Agualusa L, Lemos L, Romão J, Castro-Lopes JM: **Tradução, adaptação cultural e estudo multicêntrico de validação de instrumentos para rastreio e avaliação do impacto da dor crónica.** *Dor* 2007, **15**:6–37.
85. Roos EM, Lohmander LS: **The knee injury and osteoarthritis outcome score (KOOS): from joint injury to osteoarthritis.** *Health Qual Life Outcomes* 2003, **1**:64.
86. Goncalves RS, Cabri J, Pinheiro JP, Ferreira PL: **Cross-cultural adaptation and validation of the Portuguese version of the knee injury and osteoarthritis outcome score (KOOS).** *Osteoarthritis Cartilage* 2009, **17**:1156–1162.
87. Gandek B, Ware JE, Aaronson NK, Apolone G, Bjorner JB, Brazier JE, Bullinger M, Kaasa S, Leplege A, Prieto L, Sullivan M: **Cross-validation of item selection and scoring for the SF-12 health survey in nine countries: results from the IQOLA project.** *International Quality of Life Assessment. J Clin Epidemiol* 1998, **51**:1171–1178.
88. Wee CC, Davis RB, Hamel MB: **Comparing the SF-12 and SF-36 health status questionnaires in patients with and without obesity.** *Health Qual Life Outcomes* 2008, **6**:11.
89. Ferreira P: *Avaliação psicométrica e adaptação cultural e linguística de instrumentos de medição em saúde: princípios metodológicos gerais.* Centro de Estudos e Investigação em Saúde da Universidade de Coimbra; 1998.
90. Ferreira P: **Criação da versão Portuguesa do SF-36 - parte II - testes de validação.** *Acta Med Port* 2000, **13**:119–127.
91. Beck AT, Steer RA, Ball R, Ranieri W: **Comparison of beck depression inventories -IA and -II in psychiatric outpatients.** *J Pers Assess* 1996, **67**:588–597.
92. Campos RC, Goncalves B: **The Portuguese version of the beck depression inventory-II (BDI-II) preliminary psychometric data with two nonclinical samples.** *Eur J Psychol Assess* 2011, **27**:258–264.
93. Beck AT, Steer RA: **Internal consistencies of the original and revised beck depression inventory.** *J Clin Psychol* 1984, **40**:1365–1367.
94. Brooks D, Solway S, Gibbons WJ: **ATS statement on six-minute walk test.** *Am J Respir Crit Care Med* 2003, **167**:1287.
95. Beriault K, Carpentier AC, Gagnon C, Menard J, Baillargeon JP, Ardilouze JL, Langlois MF: **Reproducibility of the 6-minute walk test in obese adults.** *Int J Sports Med* 2009, **30**:725–727.
96. Goncalves RS, Pinheiro JP, Cabri J: **Evaluation of potentially modifiable physical factors as predictors of health status in knee osteoarthritis patients referred for physical therapy.** *Knee* 2012, **19**:373–379.
97. Bennell K, Dobson F, Hinman R: **Measures of physical performance assessments: self-paced walk test (SPWT), stair climb test (SCT), Six-minute walk test (6MWT), chair stand test (CST), timed Up & Go (TUG), sock test, lift and carry test (LCT), and car task.** *Arthritis Care Res (Hoboken)* 2011, **63**(11):S350–370.
98. Enright PL, McBurnie MA, Bittner V, Tracy RP, McNamara R, Arnold A, Newman AB: **The 6-min walk test: a quick measure of functional status in elderly adults.** *Chest* 2003, **123**:387–398.
99. Escalante Y, Garcia-Hermoso A, Saavedra JM: **Effects of exercise on functional aerobic capacity in lower limb osteoarthritis: a systematic review.** *J Sci Med Sport* 2011, **14**:190–198.
100. Schlenk EA, Lias JL, Sereika SM, Dunbar-Jacob J, Kwoh CK: **Improving physical activity and function in overweight and obese older adults with osteoarthritis of the knee: a feasibility study.** *Rehabil Nurs* 2011, **36**:32–42.
101. Jones CJ, Rikli RE, Max J, Noffal G: **The reliability and validity of a chair sit-and-reach test as a measure of hamstring flexibility in older adults.** *Res Q Exerc Sport* 1998, **69**:338–343.
102. Rikli RE, Jones CJ: **The development and validation of a functional fitness test for community-residimg older adults.** *J Aging Phys Act* 1999, **7**:129–161.
103. Bohannon RW: **Sit-to-stand test for measuring performance of lower extremity muscles.** *Percept Mot Skills* 1995, **80**:163–166.
104. Bohannon RW: **Test-retest reliability of the five-repetition sit-to-stand test: a systematic review of the literature involving adults.** *J Strength Cond Res* 2011, **25**:3205–3207.
105. Rejeski W, Miller M, Foy C, Messier S, Rapp S: **Self-efficacy and the progression of functional limitations and self-reported disability in older**

adults with knee pain. *Journal of Gerontology: Social Sciences* 2001, **56B**:S261–S265.
106. Rejeski W, Ettinger W, Schumaker S, James P, Burns R, Elam J: **Assessing performance-related disability in patients with knee osteoarthritis.** *Osteoarthritis Cartilage* 1995, **3**:157–167.
107. Rejeski W, Craven T, Ettinger W, McFarlane M, Shumaker S: **Self-efficacy and pain in disability with osteoarthritis of the knee.** *J Gerontol Psychol Sci* 1996, **51B**:P24–P29.
108. Miller M, Rejeski W, Messier S, Loeser R: **Modifiers of change in physical functioning in older adults with knee pain: the observational arthritis study in seniors (OASIS).** *Arthritis Care Res* 2001, **45**:331–339.
109. Messier S, Glasser J, Ettinger W, Craven T, Miller M: **Declines in strength and balance in older adults with chronic knee pain: A 30 month longitudinal, observational study.** *Arthritis & Rheumatism* 2002, **47**:141–148.
110. Brandt K, Heilman D, Slemenda C, Katz B, Mazzuca S, Braunstein E, Byrd D: **A comparison of lower extremity muscle strength, obesity, and depression scores in elderly subjects with knee pain with and without radiographic evidence of knee osteoarthritis.** *J Rheumatol* 2000, **27**:1937–1946.
111. Sharma L, Song J, Dunlop D, Felson D, Lewis CE, Segal N, Torner J, Cooke TD, Hietpas J, Lynch J, Nevitt M: **Varus and valgus alignment and incident and progressive knee osteoarthritis.** *Ann Rheum Dis* 2010, **69**:1940–1945.
112. Barbat-Artigas S, Rolland Y, Zamboni M, Aubertin-Leheudre M: **How to assess functional status: a new muscle quality index.** *J Nutr Health Aging* 2012, **16**:67–77.
113. Deforche B, Lefevre J, De Bourdeaudhuij I, Hills AP, Duquet W, Bouckaert J: **Physical fitness and physical activity in obese and nonobese Flemish youth.** *Obes Res* 2003, **11**:434–441.
114. Baptista F, Silva A, Marques E, Mota J, Santos R, Vale S, Ferreira J, Raimundo A, Moreira H: *Observatorio nacional da actividade física e do desporto: livro verde da aptidão física.* Lisbon, Portugal: Instituto do Desporto de Portugal (IDP); 2011. IDP.
115. Marfell-Jones M, Olds T, Stewart A, Lindsay Carter JE: *International standards for anthropometric assessment.* ISAK: Potchefstroom; 2006.
116. Lohman TG, Roche AF, Martorell R: *Anthropometric standardization reference manual champaing.* Human Kinetics Brooks: Illions; 1988.
117. Pheasant S, Haslegrave CM: *Bodyspace anthropometry, ergonomics, and the design of work.* Boca Raton, FL: Taylor and Francis; 2006.
118. Riserus U, Arnlov J, Brismar K, Zethelius B, Berglund L, Vessby B: **Sagittal abdominal diameter is a strong anthropometric marker of insulin resistance and hyperproinsulinemia in obese men.** *Diabetes Care* 2004, **27**:2041–2046.
119. Winter D: *The biomechanics and motor control of human gait: normal, elderly and pathological.* Ontario: University of Waterloo Press; 1991.
120. Block JA, Shakoor N: **The biomechanics of osteoarthritis: implications for therapy.** *Curr Rheumatol Rep* 2009, **11**:15–22.
121. Messier SP: **Osteoarthritis of the knee and associated factors of age and obesity: effects on gait.** *Med Sci Sports Exerc* 1994, **26**:1446–1452.
122. Sharma L, Hurwitz DE, Thonar EJ, Sum JA, Lenz ME, Dunlop DD, Schnitzer TJ, Kirwan-Mellis G, Andriacchi TP: **Knee adduction moment, serum hyaluronan level, and disease severity in medial tibiofemoral osteoarthritis.** *Arthritis Rheum* 1998, **41**:1233–1240.
123. Kumar D, Manal KT, Rudolph KS: **Knee joint loading during gait in healthy controls and individuals with knee osteoarthritis.** *Osteoarthritis Cartilage* 2013, **21**:298–305.
124. Teichtahl AJ, Wluka AE, Morris ME, Davis SR, Cicuttini FM: **The relationship between the knee adduction moment and knee pain in middle-aged women without radiographic osteoarthritis.** *J Rheumatol* 2006, **33**:1845–1848.
125. Thorp LE, Sumner DR, Block JA, Moisio KC, Shott S, Wimmer MA: **Knee joint loading differs in individuals with mild compared with moderate medial knee osteoarthritis.** *Arthritis Rheum* 2006, **54**:3842–3849.
126. Thorp LE, Sumner DR, Wimmer MA, Block JA: **Relationship between pain and medial knee joint loading in mild radiographic knee osteoarthritis.** *Arthritis & Rheumatism-Arthritis Care & Research* 2007, **57**:1254–1260.
127. Yamada H, Koshino T, Sakai N, Saito T: **Hip adductor muscle strength in patients with varus deformed knee.** *Clin Orthop Relat Res* 2001:179–185.
128. Craig CL, Marshall AL, Sjostrom M, Bauman AE, Booth ML, Ainsworth BE, Pratt M, Ekelund U, Yngve A, Sallis JF, Oja P: **International physical activity questionnaire: 12-country reliability and validity.** *Med Sci Sports Exerc* 2003, **35**:1381–1395.
129. Rutten A, Abu-Omar K: **Prevalence of physical activity in the European Union.** *Soz Praventivmed* 2004, **49**:281–289.
130. Rutten A, Abu-Omar K: **Perceptions of environmental opportunities for physical activity in the European Union.** *Soz Praventivmed* 2004, **49**:310–317.
131. Lee PH, Macfarlane DJ, Lam TH, Stewart SM: **Validity of the international physical activity questionnaire short form (IPAQ-SF): a systematic review.** *Int J Behav Nutr Phys Act* 2011, **8**:115.
132. *Guidelines for data processing and analysis of the international physical activity questionnaire (IPAQ)– short and long forms.* vol. 2006. https://sites.google.com/site/theipaq/, 2005.
133. Wadden TA, Foster GD: **Weight and lifestyle inventory (WALI).** *Obesity (Silver Spring)* 2006, **14**(2):99S–118S.
134. Teixeira P, Silva M: *Repensar o PESO: princípios e métodos testados para controlar o peso*; 2009.

doi:10.1186/1471-2474-14-320
Cite this article as: Yázigi *et al.*: The PICO project: aquatic exercise for knee osteoarthritis in overweight and obese individuals. *BMC Musculoskeletal Disorders* 2013 **14**:320.

Appendix 13: Yázigi F, Carnide, F. and Espanha M. Development of the Knee OA Pre-Screening Questionnaire (KOPS) (under review). *Int J Rheum Dis* 2013

International Journal of Rheumatic Diseases

DEVELOPMENT OF THE KNEE OA PRE SCREENING QUESTIONNAIRE (KOPS)

Journal:	*International Journal of Rheumatic Diseases*
Manuscript ID:	IJRD-2013-0558
Manuscript Type:	Original Article
Date Submitted by the Author:	17-Dec-2013
Complete List of Authors:	Yazigi, Flavia; Univ Lisboa, Fac Motricidade Humana, CIPER, LBMF, P-1499-00, Sports and Health Department Carnide, Filomena; Univ Lisboa, Fac Motricidade Humana, CIPER, LBMF, P-1499-00, Sports and Health Department Espanha, Margarida; Univ Lisboa, Fac Motricidade Humana, CIPER, LBMF, P-1499-00, Sports and Health Department
Keywords:	Osteoarthritis, Epidemiology < Osteoarthritis

Abstract

Self-report questionnaires are still considered to be a useful instrument for disease screening and for epidemiological studies. Few questionnaires have been developed for the purpose of screening for knee osteoarthritis (KOA). **AIM:** The aim of this study was to develop a KOA screening tool that is useful for health and exercise professionals who do not have access to advanced and costly diagnostic instruments. **METHODS:** This study comprised five steps: content validity, reliability, criterion validity, construct validity and responsiveness. Internal consistency was verified using Cronbach's alpha and the Intraclass Correlation Coefficient (ICC). Reproducibility was analyzed using the ICC (one week). Criterion validity was assessed by comparing the KOPS score *with the* SF-12, the Knee Injury and Osteoarthritis Outcome Scores questionnaire and the 6MWT. Construct validity was verified using the ROC curve (ACR clinical criteria and x-ray). Responsiveness was analyzed over 3 months of an aquatic exercise program using the pooled effect size. **RESULTS:** The overall KOPS score yielded a Cronbach's alpha of 0.747 and an ICC of 0.646. KOPS was considered reproducible (ICC: 0.895-0.992; Cronbach's alpha: 0.894-0.979). The ROC curve revealed a sensitivity of 86.96 and a specificity of 75.82. The KOPS demonstrated medium responsiveness in terms of the total score and the pain and symptoms components. **CONCLUSION:** The KOPS questionnaire is valid for the purposes for which it was created, and its translation into English should be considered.

KEYWORDS: questionnaire; construction; validation; knee; osteoarthritis; screening; KOA

1. Introduction

Knee osteoarthritis (KOA) is one of the most important public health problems in many countries[1, 2]. The situation in Portugal is similar, where the prevalence of KOA is 11.1 % (CI 95%: 9.4-13.1)[3], and it is expected that this value will increase because of the ageing of the population[4] and the rise of obesity[5]. Because of this situation, it is necessary to diagnose the condition in the early stages to manage the main symptoms and avoid disease progression.

The American College of Rheumatology (ACR) established 3 levels of diagnostic criteria for KOA: clinical only (92% sensitivity; 75% specificity), clinical and radiological (95% sensitivity; 69% specificity) or clinical and laboratorial (91% sensitivity; 86% specificity)[6]. Considering financial constraints, the clinical criteria are the most viable option for primary care.

According to the ACR clinical criteria, the KOA diagnosis should be based on the presence of knee pain in combination with at least three of the following variables: age>50, short-lived morning stiffness (<30 min), crepitus, tenderness, bony enlargement and no palpable warmth[6]. The more recent recommendations from the European League Against Rheumatism (EULAR) for clinically diagnosing KOA are based on three symptoms (persistent knee pain, morning stiffness and functional impairment) and three clinical signs (crepitus, restricted movement and bony enlargement)[7].

Laboratory and imaging methods are costly, and their associations with symptoms are not clear, particularly in the initial stages (pre-radiographic KOA, Kellgren-Lawrence radiographic grade 1)[8]. Although x-rays only provide a bone overview, the K-L severity index is considered a useful method for KOA detection in epidemiological studies[9]. Magnetic resonance imaging (MRI) is a sensitive tool that can identify joint components and some cartilage degeneration in the early stages[10, 11], but it is a very expensive technique and more studies are necessary to verify which MRI findings in early OA are clinically important[12].

For public health purposes, it is necessary to improve diagnostic instruments so that interventions can occur in earlier stages. For this purpose, self-report questionnaires are still considered a valid and accessible method for KOA screening, mainly in clinical, epidemiological and exercise field.

The available KOA-related questionnaires can be organized into two groups: patient outcomes and screening instruments. The first group includes questionnaires related to patient outcomes (functionality, signs, symptoms and quality of life)[13-18]; the Western Ontario and McMaster Universities Arthritis Index (WOMAC)[13] and the Knee Injury and Osteoarthritis Outcome Score (KOOS)[15, 19] are widely used.

The WOMAC has been validated with three types of scales: visual analog[13], Likert[13] and a numerical rating scale (NRS)[20]. The NRS allows an immediate evaluation and can be used on the phone or with a computerized touch screen (pain: ICC = 0.915, rho = 0.88; stiffness: ICC = 0.745, rho = 0.77, function: ICC = 0.940, rho = 0.87).

The KOOS is considered an extension of the WOMAC domains and is a specific instrument developed to assess patients' perceptions about their knees, their functional status and their knee-related quality of life. The KOOS was validated with a sample of 21 participants with Anterior Cruciate Ligament (ACL) injuries. Its test-retest reliability after a 9-day interval showed an ICC of 0.75 for the Daily Living subscale (ADL), 0.81 for the Sport and Recreation subscale (Sport/Rec), 0.86 for the knee-related Quality Of Life subscale (QOL), 0.85 for the Pain subscale and 0.93 for the Others Symptoms subscale[15]. The KOOS's responsiveness over 6 months was verified by assessing the effect size (QOL = 1.65; Pain = 0.84; ADL = 0.94; Symptoms = 0.87 and Sport/Recreation = 1.16)[15]. The construct validity of the KOOS was assessed in comparison to the SF-36 questionnaire[19].

Regarding the second group, there are few questionnaires related to KOA screening, possibly because the risk factors associated with KOA incidence and progression are still under discussion. In addition, failures in the validation and reliability assessment processes have prevented the development of good questionnaires [21]. In the following paragraphs, we present the main KOA-screening questionnaires that have been previously published.

The Knee and Hip Osteoarthritis Screening Questionnaire (KHOA-SQ) [22] includes 11 questions for KOA screening and different dimensions that evaluate pain, other symptoms and functionality, but it does not include risk factors in the total score, which may be one of the causes of the high false-positive rate. The validation process included 7,577 older adults (60-90 yrs) and revealed high sensitivity (94.5%) and moderate specificity (43.8%).

The Community-Oriented Program for the Control of Rheumatic Diseases (COPCORD) created the APLAR-COPCORD English questionnaire, a tool for risk factor identification[23]. Although it was used in Asia, only its content validity and reliability were checked. In addition, the authors suggested improving some items, the questionnaire shortness and performing trans-cultural validation.

The Thai Knee Osteoarthritis Screening Questionnaire (Thai-KOA-SQ)[24] addresses three factors that are associated with KOA: knee pain, age and body mass index (BMI). Although this questionnaire showed 79.2% sensitivity, 78.4% specificity and 85.1% for the area under the ROC curve (AUC), other risk factors and symptoms should be considered to guarantee that the instrument works in different populations and KOA stages.

The analyses of the existing KOA-related questionnaires reinforce the idea that, for a pre-screening questionnaire to have a consistent association with KOA, scores should include multidisciplinary factors such as the presence of signs and symptoms, physical function and risk factors. Considering that established KOA is an incurable condition, the identification of modifiable risk factors is essential to prevent incidence and progression of the disease.

The literature identifies the following risk factors as important conditions for KOA screening: external risk factors such as past sports participation, injuries, surgical interventions in the lower limbs, occupation, physical demands and lower limb strength and biological risk factors such as BMI, menopause and gender[2, 8, 11, 12, 22-25]. Among these risk factors, only BMI and strength are modifiable with lifestyle changes.

In the predictive models presented by Zhang et al. (2011)[25], age, sex, BMI, occupation, family, and knee injuries were risk factors related to KOA incidence (AUC of ROC curve ranged from 0.55 to 0.81), and age, sex, knee injuries and sports were the risk factors related to KOA progression (AUC of ROC curve ranged from 0.45-0.82).

With regard to self-reported questionnaires, it is important to verify that they are user-friendly. Therefore, they should not be too long and should not have too many issues that may not be easily understood. In addition, the questions should be simple and clear: participants should be able to answer the questions without the assistance of a specialist or expert.

The aim of this study was to develop a KOA instrument that is useful for KOA screening and for health and exercise professionals so that imaging and other expensive resources are not needed. Thus, the specific objectives of this study were to develop a KOA screening questionnaire, to create consensus criteria for early KOA diagnosis and to develop a scoring system for accurate KOA diagnosis.

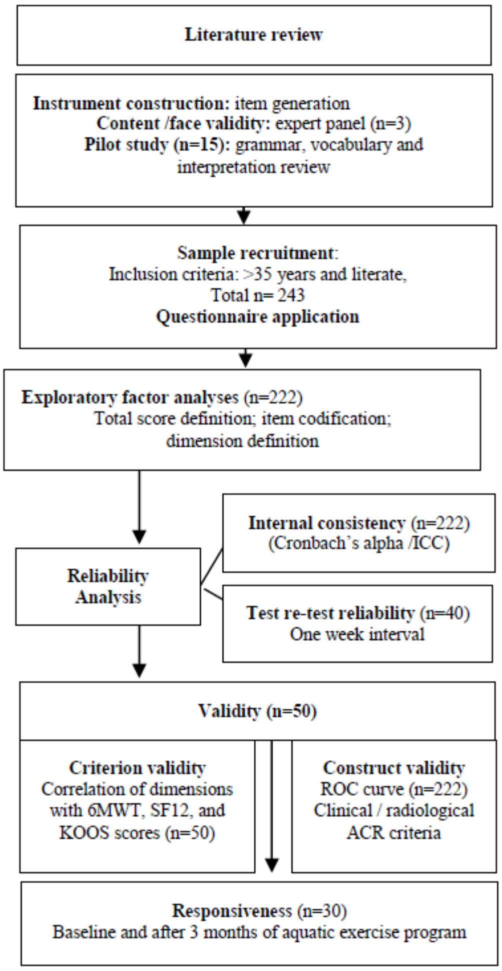
2. Study design and setting

This study comprised five phases: content validity, reliability, criterion validity, construct validity and responsiveness: content validity, reliability (internal consistency and reproducibility), criterion validity, construct validity and responsiveness (Fig 1). The study is part of the PICO project (Intervention Program Against Osteoarthritis, Clinical Trial Registration: NCT01832545), which was approved by the Ethical Committee of the Faculty of Human Kinetics at the University of Lisbon and was already published[26].

2.1. Sample

The subjects were recruited through newspaper announcements and community centers. To detect KOA in progress (KL ≥1 grade)[25], the inclusion criteria were an age ≥ 35 years and the ability to read and write. Although the ACR clinical criteria for the KOA diagnosis include an age limit of ≥50 years old, because of the increase in other risk factors, such as obesity, recent studies have reported KOA at early ages[7, 27]. Thus, the age inclusion criterion of ≥35 years was established to guarantee the ability of the KOPS to detect KOA in a broader age group.

The exclusion criterion was any cognitive/mental impairment that could compromise the understanding of the questionnaire or the quality of self-reported information. A total of 243 volunteers signed the informed consent form and were included in different phases of the validation process.



Abbreviations: ICC = Intra Class Coefficient; KOOS = knee injury and osteoarthritis outcome score; SF12= Health Survey; 6MWT= six minutes walking test

Fig 1. Flow chart of the KOPS construction and validation process

2.2. Procedures and statistical analyses

Instrument development and content validity

The KOPS development and item selection followed a structured process which was supported by an exhaustive literature review, the ACR and EULAR criteria for KOA [6, 7], the validation process for published screening questionnaires[22-24] and the analyses of the WOMAC[13] and the KOOS[15]. The items selection was critically defined by panel of experts, namely two rheumatologists, one physiotherapist, one epidemiologist and one sports science specialist.

So, the first version of the questionnaire included demographics and 13 questions organized into three sections: risk factors (female sex, age, body mass index, lower limb injuries, sports activity and working posture), signs and symptoms (stiffness, crepitus, restricted movement, pain and deformity) and physical function. During this phase, two similar questions about pain intensity were included to determine which pain scale was more accurate: one scale was the 0–10 pain intensity (NRS), and the other was the visual analogue scale (VAS).

This version was tested by performing a pilot study with 15 participants and by consulting the mentioned expert panel. Self-reported answers were confirmed in an interview to verify the Portuguese grammar and semantics, to check the clarity and relevance of the questions, to assure that all essential concepts were included correctly and to guarantee that all of the items related to the objectives were appropriate and comprehensible.

Once the final version was produced, the load for each item was determined to construct a total score to measure the latent variable. To avoid an overload of some items, the discrete variables (age, BMI and the amount of years in sports) were transformed into ordinal variables. Age (years) was categorized into seven intervals ($\leq$ 39 = 0; 40-49 = 1; 50-59 = 2; 60-69 = 3; 70-79 = 4; 80-89 = 5; $\geq$ 90 = 6); BMI was categorized into 6 intervals (underweight = 1; healthy = 2; overweight = 3; grade 1 obesity = 4; grade 2 obesity = 5 and grade 3 obesity = 6)[28]; and sports volume (years X weekly frequency of sports activity) was categorized into 7 intervals (0 = no sports; 1 = 1-15; 2 = 16-29; 3 = 30-44; 4 = 45-59; 5 = 60-74; 6 = 75-89; 7 $\geq$ 90 points).

An exploratory factor analysis was used to verify the item-content agreement[29]. The sampling adequacy for factorial analyses was verified using the Kaiser-Meyer-Olkin test (KMO) [30], and sphericity was determined using Bartlett's test[31]. A principal component analysis with varimax rotation was used.

Reliability and validity

The reliability of the KOPS was verified by assessing the internal consistency (IC) (n= 222) with two techniques:

a) Cronbach's alpha coefficient. Reliability is considered acceptable for group comparisons when Cronbach's alpha exceeds 0.8 [32]. Item-total correlations were applied between item scores and the total KOPS score, and correlations $\leq$ 0.4 were rejected [33].

b) The Intraclass Correlation Coefficient (ICC) was used to measure inter-rater reliability. When the correlations were $\geq$0.90, items were considered redundant and were removed from the questionnaire[32, 34].

Reproducibility

Reproducibility was verified in a test-retest study in which 40 individuals completed the questionnaire at two moments within a one-week interval. The reproducibility of the total KOPS score and the six components were compared by calculating the ICC[35].

Criteria and construct validity

The convergent criterion validity was assessed by comparing the KOPS components' scores with the SF-12v2 Health Survey [Mental Component (MCS) and Physical Component (PCS) scores] 36 and the KOOS questionnaire15. In addition, Spearman's Coefficient (Rho) was used to analyze the correlation between the KOPS and the 6MWT37. Fifty participants were included in this process.

For construct validity, the sensitivity and specificity of the KOPS were verified by assessing the ROC curve. The following questions were analyzed: (1) Do the participants who self-reported a high score potentially have knee OA? (2) Is the KOPS a good instrument for diagnosing KOA? (3) Is there a cut-off KOPS score that indicates the presence of KOA?

For this study, 222 individuals (69 with clinical and radiological diagnosis of KOA) were recruited across the PICO project[26]. The KOPS scores were compared with the ACR clinical and radiological diagnosis[6]. In addition, the ROC curve was used to find the cut-off KOPS score with the best sensitivity and specificity for diagnosing KOA. The confidence interval for the AUC was established at 95% [38].

Responsiveness

Even though the KOPS questionnaire was created to be a screening instrument, its responsiveness was analyzed to verify whether it could be used for longitudinal studies.

The capacity to detect clinically important changes over 3 months of the aquatic Intervention Program Against Osteoarthritis (PICO) was analyzed by determining the pooled effect size (ES), Cohen's d. The KOPS scores of 30 obese patients with KOA were compared. The significance level was set at $P < 0.05$[39].

The data analysis was carried out using the statistical program IBM SPSS Statistics 21, and the Receiver Operating Characteristic (ROC) curve analysis and ES analysis were performed using Med Calc software.

3. Results

The sociodemographic characteristics and working conditions of the participants who were included in the validation process are shown in Table 1.

Table 1. Sample characteristics at different phases of the validation process.

	Content validity (n=222)	Reliability (n=40)	Construct validity (n=50)
Variables	mean(SD);median	mean(SD);median	mean(SD);median
Age (yrs)	53.3(11.6); 53.5	52.1(8.7); 50.5	55.4(6.1); 56
Body Mass (Kg)	79.3(17.6); 79	68.6(15.4); 65	91.4(13.4); 91
Height (m)	1.63(0.09); 1.62	1.61(0.08); 1.60	1.60(0.1); 1.60
BMI (Kg/m^2)	29.7(6.1); 29.2	26.5(5.5); 24.6	35.6(5.1); 33.4
	***n* (%)**	***n* (%)**	***n* (%)**
Sex			
Female	167 (75.2)	33 (82.5)	35(71.4)
Male	55(24.8)	7(17.5)	14(28.6)
Age Group (years)			
≤39	36 (16.2)	1 (2.5)	0
40-49	72(32.4)	17(42.5)	9(18.4)
50-59	62(27.9)	16(40)	26(52.0)
60-69	34 (15.3)	5 (12.5)	15(30.0)
>69	18 (8.1)	1(2.5)	0
Job Posture			
Standing position	105(57.1)	16(45.7)	44(89.8)
Sitting position	108(58.7)	21(60)	30(68.2)
Squatting position	40(21.7)	1(2.9)	6(13.6)
Educational Level			
Reading/writing	2(0.9)	0	0
Elementary school	31(14.0)	6(15.8)	6(12.0)
High school grade 9-12	34(15.4)	4(10.5)	8(16.0)
High school graduate	53(24.0)	10(26.3)	13(26.0)
College	101(45.7)	18(47.4)	23(46.0)

Abbreviations: BMI =body mass index; SD = standard deviation

KOPS characterization

After the pilot study, the main changes adopted in the instrument were as follows: 1) introduction of a new risk factor: Sports Volume; 2) separation of the stiffness question in two questions: morning stiffness and position stiffness; 3) development of a filter to organize the order of the questions and facilitate understanding; and 4) removal of the Likert scales associated with stiffness, creaking, swelling and functional limitations because the experts concluded that this information was more important for assessing functional status than for identifying KOA. In the response options, the term "sometimes" was included to facilitate the respondent's task (for codification, it was counted as a "yes"). For the knee pain questions, the NRS was maintained to obtain additional information about pain intensity, which is considered the main symptom and a cause of lower levels of physical activity.

The final version of the KOPS was a self-report questionnaire composed of closed-ended questions with nominal and ordinal response options. The first part includes sociodemographic information, the second part has risk factor information, the third part is about signs and symptoms and the last part has additional information related to mobility, exercise and clinical supervision. The KOPS takes approximately 9±4 minutes to fill out.

3.1. Factorial Analyses

A total of 10 items were eliminated because they did not contribute to a simple factor structure and failed to meet the minimum criterion of having a primary factor loading of 0.4 or higher[29]. The KMO measure of sampling adequacy was good (0.774, above the commonly recommended value of 0.6)[30]. Bartlett's test of sphericity was significant (χ^2 (153) = 492.84, $P < 0.001$).

Factorial analyses were performed for 3, 4, 5, 6 and 7 components. The best loadings were found for 6 components organized in two dimensions: symptoms (49.1% of variance) and risk factors (18.5% of variance). The factor-loading matrix for this final solution is presented in Table 2.

Table 2. Confirmatory factor analyses: Components' loading for rotated component matrix.

	Dimensions	
Components	**Symptoms**	**Risk factors**
Pain on function	0.849	0.095
Signs/others symptoms	0.817	0.065
Pain intensity (last month)	0.861	0.002
Pain intensity (last year)	0.857	0.011
Biological risk	0.274	0.671
External risk	0.174	0.816
% of variance explained	49.10	18.50

How is the KOPS scored? (Table 3)

The maximum value that could be scored on the KOPS is 54; as the value increases from zero, there is a greater possibility of having knee OA.

Functional pain and the Signs and Other symptom components were scored from 0-1, with one representing a positive answer; both pain components were scored from 0-10.

In the biological risk component, age was scored from 0-6, menopause was scored from 0-1 (with one representing being in menopause) and BMI was scored from 0-6. Finally, the external risk component, lower body injury and job posture were scored from 0-1, and sports volume was scored from 0-7.

Table 3. Dimensions, components, items and maximal scores of the KOPS questionnaire.

Dimensions (2)	Components (6)	Items (18)	Score
Symptom	Functional Pain (FP)		4
		Walking pain	1
		Standing position	1
		Stepping pain	1
		Chair pain	1
	Pain intensity - month (MP)	Last month	10
	Pain intensity-year (YP)	Last year	10
	Signs/others symptoms (SOS)		6
		Morning stiffness	1
		Position stiffness	1
		Swelling	1
		Creaking	1
		Knee extension	1
		Deformity	1
Risk factors	Biological risk (BR)		13
		Age interval	6
		Menopause	1
		BMI classification	6
	External risk (ER)		11
		Lower limb injury	1
		Job posture: stand position	1
		Job posture: sitting position	1
		Job posture: squat position	1
		Sports volume	7
KOPS total score			**54**

3.2. Reliability

The mean KOPS score for the 222 participants in the reliability study was 16.2, ranging from 4-38. The descriptive statistics (mean; SD) for each component were as follows: Functional Pain (1.4; 1.5), Pain intensity/month (2.2; 3.0), Pain Intensity/year (3.0; 3.1), Signs/other symptoms (2.0; 1.8), Biological risk (2.2; 1.7) and External risk (2.2; 1.7).

The internal consistency (IC) analysis revealed acceptable reliability of the KOPS score with a Cronbach's alpha of 0.747 and a satisfactory ICC (an average of 0.646). The reproducibility results are expressed in Table 4. The results for the test-retest over a one-week interval for each component ranged from 0.895-0.992 for the ICC and from 0.894 to 0.979 for Cronbach's alpha.

Table 4. ICC and Cronbach's alpha for reproducibility analyses of each component

Components	**ICC**	**Cronbach's Alpha**
Functional pain	0.895	0.894
Pain last month	0.967	0.970
Pain last year	0.965	0.970
Signs/other symptoms	0.925	0.923
Biological risk	0.992	0.992
External risk	0.904	0.903
KOPS total score	**0.977**	**0.979**

3.3. Criteria and construct validity

The associations between the KOPS score and the KOOS, the SF-12 and the results from the 6MWT were investigated by calculating the Spearman Coefficient (Table 5). The total KOPS score showed a moderate negative correlation with the SF-12 PCS (r =-0.443; P = 0.001) and all of the KOOS dimensions except KOOS Pain, which had a strong association (r = - 0.717; P = 0.000). The SF-12 MCS did not show a significant correlation with KOPS. Among the risk factors, only the biological risk component showed a significant association with the gold standard instruments (i.e., the 6MWT and the SF12 PCS).

Table 5. Spearman's correlation coefficients (KOPS is 0–54 points, best to worst; SF-12 is 0–100 points, worst to best; KOOS is 0-100 points, worst to best).

KOPS Components	SF-12 PCS	SF-12 MCS	6MWT	KOOS Pain	KOOS Symptoms	KOOS ADL	KOOS Sport/Rec	KOOS QOL
KOPS signs/ other symptom	-0.201	-0.247	-0.488 [b]	-0.564 [b]	-0.617 [b]	-0.413 [a]	-0.344 [a]	-0.295 [a]
KOPS biological risk	-0.417 [a]	-0.030	-0.423 [a]	-0.163	-0.242	-0.301 [a]	-0.048	-0.157
KOPS external risk	0.140	-0.208	0.157	-0.108	-0.144	0.040	-0.084	-0.255
KOPS month pain	-0.457 [b]	-0.125	-0.284 [a]	-0.623 [b]	-0.505 [b]	-0.363 [a]	-0.470 [b]	-0.605 [b]
KOPS year pain	-0.381 [a]	-0.190	-0.380 [a]	-0.633 [b]	-0.481 [b]	-0.368 [a]	-0.466 [b]	-0.597 [b]
KOPS functional pain	-0.413 [a]	-0.020	-0.109	-0.310 [a]	-0.321 [a]	-0.272	-0.293 [a]	-0.390 [a]
KOPS Total	-0.443 [a]	-0.239	-0.415 [a]	-0.717 [b]	-0.615 [b]	-0.454 [b]	-0.500 [b]	-0.662 [b]

Abbreviations: 6MWT, six-minute walking test; PCS, physical component score; MCS, mental component score.

a level of significance $p < 0.05$.
b level of significance $p < 0.001$.

An ROC curve analysis was performed to evaluate the sensitivity and the specificity of the KOPS in comparison with ACR clinical and radiological criteria for KOA diagnosis. The ROC curve revealed a KOPS score of 16 with sensitivity of 86.96, specificity of 75.82 and an AUC of 0.880 ($P < 0.001$).

3.4. Responsiveness

In general, the pooled ES (Cohen's d) demonstrated the ability of the KOPS to detect changes after 3 months of an aquatic exercise program for 30 obese adults with KOA. Better ES were observed for the total score (d = 0.349) and for 3 components: signs/other symptoms (d = 0.483), knee pain in the past month (d = 0.657) and functional pain (d = 0.318). Less responsiveness was found for biological and external risk components (d = 0.076 and d = 0.000, respectively) and for knee pain in the past year (d = 0.174).

4. Discussion

The major strength of our study was that we designed a KOA screening questionnaire with a complete validation process, including assessments of reproducibility and responsiveness, two important steps that are sometimes not completed because they require more complex procedures.

KOPS was developed for use in KOA screening situations before radiologic diagnostic tests. The KOPS proved to be user-friendly and quick to complete. Furthermore, it did not require specialist supervision, unlike APLAR-COPCORD English questionnaire[23],, which will facilitate its use by exercise instructors, physicians, nurses and other professionals.

9

In contrast with the KHOA-SQ validation[22], the KOPS has more questions (24 vs 11), but it is more inclusive and applicable to a larger age group (≥35 yrs). It also includes a risk factor dimension, which is an important aspect. Although the sample size for the validation process was smaller than for the KHOA (222 vs 7577), the KOPS had a sample with diverse characteristics, thus supporting the use of the KOPS in different populations.

In comparison with other questionnaires[13, 15, 23, 24], the KOPS is innovative because it includes KOA risk factors in the total score, which may explain the good validity and reliability results obtained in the present study. The factorial analyses revealed a good balance among the loads of the components, and both dimensions explained 67.6% of the variance, which is close to the desired variance in this type of validation process (70%). The ICC and Cronbach's alpha (0.646 and 0.747, respectively) values were comparable to the values obtained in the validation of the KOOS and the WOMAC, two reputable questionnaires.

The questionnaire showed good reproducibility. The high ICC values shown in Table 4 were expected for all signs, symptoms and risk factors except for components related to pain, which typically show greater variability in self-reported conditions. These results can be explained because the questions about other symptoms referred to the last month and the year before, which does not allow for substantial variation in a week. It is important to note that most of the risk factors included in the KOPS items are not modifiable factors.

In comparison with the pre-defined gold standard (KOOS, SF12 and the functional test (6MWT), the KOPS demonstrated good criterion validity. Higher correlations were found between the total KOPS score and the KOOS than between the KOPS and the SF12, mainly for pain, other symptoms and quality of life. These results could be explained by the fact that the KOOS is a specific tool for KOA, whereas the SF12 involves general physical and mental health outcomes. As in the KOOS validation, (when compared with the SF-36), better associations was found between the KOPS and the SF-12 physical component than the mental component. The lower correlation between external risk on the KOPS and the SF12- PCS was expected because they are independent variables: sports participation, surgery and jobs performed in the past might not have any direct relationship with physical function in the present. In addition, our data indicate that the biological risk factors for KOA (BMI and age) are inversely associated with the SF-12 physical function component.

Regarding the ability of the KOPS to assess physical function related to KOA symptoms, beyond the comparison with the SF12, the 6MWT was chosen because it is a valid and direct measure that provides a real asset for assessing the convergent validity of the KOPS. An inverse correlation ranging from 0.4 to 0.5 ($P < 0.05$) was found when the results of the 6MWT were compared with the KOPS total score, with signs/others symptoms and biological risk components. The two first correlations were expected because KOA symptoms compromise the ability to walk. The correlation between 6MWT and biological risk factors is interesting and can be explained by BMI and age.

One advantage of this study is that it was possible to verify the construct validity by comparing the KOPS score with the radiological diagnosis only and with the ACR's clinical and radiological criteria for KOA. Although there is much discussion in the medical community about what is considered the gold standard, the ACR criteria still provide a conservative and valid reference. Therefore, the hypothesis formulated in this process was confirmed: both areas under the ROC curve were above 0.850, higher than the predictive models presented by Zhang et al. (2011)[25] and similar to the AUC for the Thai-HOA-SQ[24]. Regarding sensitivity and specificity, the KOPS values for clinical and radiological diagnosis had a higher sensitivity and slightly lower specificity compared to the Thai-KOA-SQ (79.2%; 78.4%), a lower sensitivity (87.0 vs 94.5%) and a much higher specificity (75.8 vs 43.8%) in comparison with the KHOA-SQ. The lower sensitivity could be related to the smaller sample size in our study. These results clearly show that the total KOPS score can distinguish individuals with KOA from others without KOA, indicating that this instrument has valid constructs.

The suggested threshold value with the highest specificity/sensitivity is 16, which means that participants with a KOPS score ≥16 had a greater probability of KOA, the latent variable. The inclusion of risk factors, according to the EULAR recommendations[7], might have contributed to the strong specificity for detecting the presence of KOA, mainly in special populations that often have other comorbidities.

The ES for responsiveness revealed medium sensitivity for change in some components, mainly the short-term modifiable components such as pain in the last month, functional pain and other symptoms. External risk factors such as surgery, sports or occupational activity in the past are not modifiable risks, so no changes were expected. Likewise, self-reported pain in the past year was not expected to change after the 3-month intervention because the reported pain was in the last year and not in the present. The KOPS detected improvements from the exercise intervention in self-reported pain in the last month and in other symptoms such as stiffness, swelling and functionality. Unlike the KOOS [19], the total KOPS score has a weak sensitivity to change, which can be explained because the former was created to measure treatment outcomes and the latter was created for screening, with many components related to unchangeable outcomes.

5. Conclusion

In summary, the present study confirms the utility and accuracy of the KOPS questionnaire for KOA screening in epidemiological studies and for exercise and health professionals who need to screen KOA for their intervention, specifically for exercise prescriptions.

The KOPS was constructed and validated for a Portuguese population. Given the good results, the authors agree that the KOPS can be a very useful instrument and that future studies validate the instrument in English. In addition, a larger sample size in the validation process will enable the use of the KOPS for different populations.

Acknowledgements

The authors give special thanks to the PESO Comunitario, Dr. Pedro Teixeira, Dr. Raul Oliveira, the Portuguese Institute of Rheumatology and others institutions that allowed the application of the questionnaires.

Conflict of interest statement

The authors declare no commercial relationships or conflicts of interest.

Authors' Contributions

Flávia Yázigi and Filomena Carnide worked on the design, analysis and interpretation, drafting and revision and approved the final version. Margarida Espanha contributed to the design, patient recruitment and revision and gave final approval.

References

1. Zhang Y, Jordan JM. Epidemiology of osteoarthritis. Clin Geriatr Med. 2010;26(3):355-69. Epub 2010/08/12.
2. Jordan JM, Helmick CG, Renner JB, Luta G, Dragomir AD, Woodard J, et al. Prevalence of knee symptoms and radiographic and symptomatic knee osteoarthritis in African Americans and Caucasians: the Johnston County Osteoarthritis Project. The Journal of rheumatology. 2007;34(1):172-80. Epub 2007/01/12.
3. Costa L, Gal D, Barros H. Prevalence of rheumatic diseases in an urban population. Acta Reum Port29:169-174. 2004(29):169-74.
4. Instituto Nacional de Estatística (INE). Censos - Resultados definitivos : Portugal - 2011 Lisbon: INE - Statistics Portugal; 2012.
5. do Carmo I, Dos Santos O, Camolas J, Vieira J, Carreira M, Medina L, et al. Overweight and obesity in Portugal: national prevalence in 2003-2005. Obesity reviews : an official journal of the International Association for the Study of Obesity. 2008;9(1):11-9. Epub 2007/11/24.
6. Altman RD. Criteria for the classification of osteoarthritis of the knee and hip. Scand J Rheumatol Suppl. 1987;65:31-9. Epub 1987/01/01.
7. Zhang W, Doherty M, Peat G, Bierma-Zeinstra MA, Arden NK, Bresnihan B, et al. EULAR evidence-based recommendations for the diagnosis of knee osteoarthritis. Annals of the rheumatic diseases. 2010;69(3):483-9. Epub 2009/09/19.
8. Rajabi R, Johnson GM, Alizadeh MH, Meghdadi N. Radiographic knee osteoarthritis in ex-elite table tennis players. BMC musculoskeletal disorders. 2012;13:12. Epub 2012/02/09.
9. Horvath G, Koroknai G, Acs B, Than P, Bellyei A, Illes T. Prevalence of radiographic primary hip and knee osteoarthritis in a representative Central European population. International orthopaedics. 2011;35(7):971-5. Epub 2010/06/18.
10. Ai F, Yu C, Zhang W, Morelli JN, Kacher D, Li X. MR imaging of knee osteoarthritis and correlation of findings with reported patient pain. J Huazhong Univ Sci Technolog Med Sci.30(2):248-54. Epub 2010/04/22.
11. Cibere J, Zhang H, Thorne A, Wong H, Singer J, Kopec JA, et al. Association of clinical findings with pre-radiographic and radiographic knee osteoarthritis in a population-based study. Arthritis care & research.62(12):1691-8. Epub 2010/07/29.
12. Javaid MK, Lynch JA, Tolstykh I, Guermazi A, Roemer F, Aliabadi P, et al. Pre-radiographic MRI findings are associated with onset of knee symptoms: the most study. Osteoarthritis and cartilage / OARS, Osteoarthritis Research Society.18(3):323-8. Epub 2009/11/19.
13. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. The Journal of rheumatology. 1988;15(12):1833-40. Epub 1988/12/01.

14. Goncalves RS, Cabri J, Pinheiro JP, Ferreira PL, Gil J. Reliability, validity and responsiveness of the Portuguese version of the Knee injury and Osteoarthritis Outcome Score--Physical Function Short-form (KOOS-PS). Osteoarthritis and cartilage / OARS, Osteoarthritis Research Society.18(3):372-6. Epub 2009/11/17.
15. Roos EM, Roos HP, Lohmander LS, Ekdahl C, Beynnon BD. Knee Injury and Osteoarthritis Outcome Score (KOOS)--development of a self-administered outcome measure. The Journal of orthopaedic and sports physical therapy. 1998;28(2):88-96. Epub 1998/08/12.
16. Rat AC, Coste J, Pouchot J, Baumann M, Spitz E, Retel-Rude N, et al. OAKHQOL: a new instrument to measure quality of life in knee and hip osteoarthritis. Journal of clinical epidemiology. 2005;58(1):47-55. Epub 2005/01/15.
17. Bellamy N, Bell MJ, Pericak D, Goldsmith CH, Torrance GW, Raynauld JP, et al. BLISS index for analyzing knee osteoarthritis trials data. Journal of clinical epidemiology. 2007;60(2):124-32. Epub 2007/01/09.
18. Greco NJ, Anderson AF, Mann BJ, Cole BJ, Farr J, Nissen CW, et al. Responsiveness of the International Knee Documentation Committee Subjective Knee Form in comparison to the Western Ontario and McMaster Universities Osteoarthritis Index, modified Cincinnati Knee Rating System, and Short Form 36 in patients with focal articular cartilage defects. The American journal of sports medicine.38(5):891-902. Epub 2010/01/02.
19. Roos EM, Toksvig-Larsen S. Knee injury and Osteoarthritis Outcome Score (KOOS) - validation and comparison to the WOMAC in total knee replacement. Health and quality of life outcomes. 2003;1:17. Epub 2003/06/13.
20. Theiler R, Spielberger J, Bischoff HA, Bellamy N, Huber J, Kroesen S. Clinical evaluation of the WOMAC 3.0 OA Index in numeric rating scale format using a computerized touch screen version. Osteoarthritis and cartilage / OARS, Osteoarthritis Research Society. 2002;10(6):479-81. Epub 2002/06/12.
21. Olsen J. Epidemiology deserves better questionnaires. IEA European Questionnaire Group. International Epidemiological Association. Int J Epidemiol. 1998;27(6):935. Epub 1999/02/19.
22. Quintana JM, Arostegui I, Escobar A, Lafuente I, Arenaza JC, Garcia I, et al. Validation of a screening questionnaire for hip and knee osteoarthritis in old people. BMC musculoskeletal disorders. 2007;8:84. Epub 2007/08/25.
23. Haq SA, Davatchi F, Dahaghin S, Islam N, Ghose A, Darmawan J, et al. Development of a questionnaire for identification of the risk factors for osteoarthritis of the knees in developing countries. A pilot study in Iran and Bangladesh. An ILAR-COPCORD phase III study. International journal of rheumatic diseases. 2010;13(3):203-14. Epub 2010/08/14.
24. Satayavongthip B, Kerdchantuk P, Hanrinth R, Methieng T, Khunpimul P. Development of the Thai Knee Osteoarthritis Screening Questionnaire (Thai-KOA-SQ) in Kanleumg Sub-District, Nakronpanom Province. Journal of the Medical Association of Thailand = Chotmaihet thangphaet. 2011;94(8):947-51. Epub 2011/08/26.
25. Zhang W, McWilliams DF, Ingham SL, Doherty SA, Muthuri S, Muir KR, et al. Nottingham knee osteoarthritis risk prediction models. Annals of the rheumatic diseases. 2011;70(9):1599-604. Epub 2011/05/27.
26. Yazigi F, Espanha M, Vieira F, Messier SP, Monteiro C, Veloso AP. The PICO project: aquatic exercise for knee osteoarthritis in overweight and obese individuals. BMC musculoskeletal disorders. 2013;14(1):320. Epub 2013/11/14.
27. Neogi T, Zhang Y. Epidemiology of osteoarthritis. Rheumatic diseases clinics of North America. 2013;39(1):1-19. Epub 2013/01/15.
28. American College of Sports Medicine (ACSM). ACSM's Guidelines for Exercise Testing and Prescription. 8th ed: Lippincott Williams & Wilkins; 2009.
29. Jolliffe IT. Sample sizes and the central limit theorem: The Poisson distribution as an illustration - Reply. American Statistician. 1996;50(3):282-.
30. Kaiser H. A second generation little jiffy. Psychometrika. 1970;35(4):401-15.
31. Bartlett M. Tests of significance in factor analysis. 3(Part II):77-85. British Journal of Psychology. 1950;3(Part II):77-85.
32. Nunnally J, Bernstein I. Psychometric Theory 3rd ed. New York: McGraw Hill; 1994.
33. Kline P. A handbook of test construction: Introduction to psychometric design. : New York: Methuen; 1986.
34. Terwee CB, Bot SD, de Boer MR, van der Windt DA, Knol DL, Dekker J, et al. Quality criteria were proposed for measurement properties of health status questionnaires. Journal of clinical epidemiology. 2007;60(1):34-42. Epub 2006/12/13.
35. Shrout PE, Fleiss JL. Intraclass correlations: uses in assessing rater reliability. Psychol Bull. 1979;86(2):420-8. Epub 1979/03/01.
36. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care. 1996;34(3):220-33. Epub 1996/03/01.
37. Brooks D, Solway S, Gibbons WJ. ATS statement on six-minute walk test. Am J Respir Crit Care Med. 2003;167(9):1287.
38. DeLong E, DeLong D, Clarke-Pearson D. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. Biometrics. 1998;44:837-45.
39. Husted JA, Cook RJ, Farewell VT, Gladman DD. Methods for assessing responsiveness: a critical review and recommendations. Journal of clinical epidemiology. 2000;53(5):459-68. Epub 2000/05/17.

Appendix 14: Yázigi, F, Espanha, M., Marques, A., Vitorino, J., Silva, I., Sousa, M., & Cunha, C. (2012). Predictive Factors of 6MW Test in Obese Individuals with Knee OA (abstract). Acta Reumatol Port, 37(Suppl), 66-67.

XVI CONGRESSO PORTUGUÊS DE REUMATOLOGIA

Comunicações orais

ACTA REUMATOL PORT. 2012:37:55-69 (SUP)

CO14 – PREDICTIVE FACTORS OF THE SIX MINUTES WALKING TEST IN OBESE INDIVIDUALS WITH KNEE OA

Yázigi F[1], Espanha M[1], Marques A[1], Cunha C[2], Vitorino J[2], Monge I[2], Sousa M[3]
1. Interdisciplinary Centre for the Study of Human Performance (CIPER), Faculty of Human Kinetics, Technical University of Lisbon;
2. Faculty of Human Kinetics, Technical University of Lisbon;
3. Portuguese Institute of Rheumatology

Knee Osteoarthritis (KOA) is increasing, due in part to obesity making it one of the most common causes of disability. Knee loads related to obesity and joint weight-bearing plays an important role in the development and progression of KOA. Besides, knee pain is a common complaint among obese individuals compromising joint mobility and therefore physical function. One of the most important functional assessments for KOA individuals is walking capacity which might be done using the Six Minute Walk Test (6MWT). This test has been referred as a reliable test to predict functional capacity in individuals with symptomatic KOA.
Purpose: the purpose of this study was to determine which factors might predict the performance of the 6MWT in obese individuals with KOA.
Methods: From 80 obese volunteers with sympto-

matic KOA, 50 adults (35 women, 15 men) with radiographic KOA were included (age: 55.3±6.7yrs; Body Mass Index (BMI): 34.9±4.9Kg m^{-2}) in this study. Self-report measures were recorded by using the Knee Injury and Osteoarthritis Outcome Score (KOOS) Pain and Other Symptoms subscales, the Beck Depression Inventory (BDI) and the International Physical Activity Questionnaire, short version (IPAQ) to control the amount of physical activity. Functional tests included the 6MWT, balance test (stand on foam with eyes closed) and Five-Times-Sit-to-Stand Test (FTSST). Pearson's coefficient was used to analyze the correlation between age, BMI, distance of 6MWT, impact of pain on activities of daily living, other knee symptoms, depression, balance, and lower extremity muscle performance. Multiple regression analyses (stepwise) were used to identify which factors best predict the 6MWT.

Results: Pearson's correlation showed that 6MWT was inversely correlated with knee pain (r=-.535, p<.001), with BMI (r=-.421, p=.002), and with BDI score (r-.455, p=.001), and positively correlated with the FTSST (r=.413, p=.003). The Stepwise multiples regression analysis revealed that the significant predictors of 6MWT were KOOS pain subscale, BDI score, and FTSST (adjusted R^2=0.421, p<.001). Additionally, separate analyses for sex were done showing that only one factor significantly predicted the 6MWT. For men the FTSST explained 64% of the variance obtained in the 6MWT (p<.001) and for women the unique predictor was the KOOS other symptoms subscale (adjusted R^2=0.245, p=.001).

Conclusions: Negative association between 6MWT and BMI was somehow expected, as obese individuals suffer higher joint stress showing poor walking ability. However, BMI in this regression model did not explain the walked distance, probably because all the subjects in this study were obese. Our findings suggest that higher knee pain and lower limb strength were associated with a lower functional capacity. Muscle weakness is considered part of the mechanical pathology of KOA and pain has mostly a mechanical pattern, affecting postural control required in walking. Depression state was also related to walking ability, showing that attitudes and beliefs negatively reflected in the capability of accomplishing this physical task. The lower limb strength explained the walking ability in men, but this finding should be considered cautiously due to the small number of individuals. Finally, the women's perceived knee health status moderately explains the performance in this walking test.